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INDEX TO EXHIBITS

A. Affidavit of Jennifer K. Squillario

B. Subpoena Issued to Archives of Internal Medicine

C. Subpoena Issued to the Journal of the American Medical Association

D. November 19, 2007 Memorandum and Order Re: Motions to Exclude Expert Testimony

E. September 7, 2007 Letter from Joseph P. Thorton to Jennifer K. Squillario and June 8, 2007 e-mail from Joseph P. Thorton to Heather R. Olson and Matthew J. Sullivan

F. September 14, 2007 Letter from Joseph P. Thorton to Jennifer K. Squillario

G. September 21, 2007 Letter from Jennifer K. Squillario to Joseph P. Thorton

H. October 26, 2007 E-mail from Joseph P. Thorton to Jennifer K. Squillario

I. November 19, 2007 Letter from Jennifer K. Squillario to Joseph P. Thorton

J. January 11, 2008 Letter from Joseph P. Thorton to Jennifer K. Squillario

EXHIBIT A

IN THE UNITED STATES DISTRICT COURT
FOR THE NORTHERN DISTRICT OF ILLINOIS

IN RE BEXTRA AND CELEBREX MARKETING SALES PRACTICES AND PRODUCT LIABILITY LITIGATION	Civil Case No.: _____
	Related Case Number M:05-cv-01699-CRB MDL No. 1699 Pending in the Northern District of California, San Francisco Division

DECLARATION OF JENNIFER SQUILLARIO, ESQ. IN SUPPORT OF MOTION TO COMPEL PRODUCTION OF DOCUMENTS FROM NON-PARTIES THE AMERICAN MEDICAL ASSOCIATION, THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION AND THE ARCHIVES OF INTERNAL MEDICINE

By this declaration, Jennifer K. Squillario declares as follows:

1. I am one of the attorneys representing Pfizer Inc. in the multi-district litigation, *In re Bextra and Celebrex Marketing Sales Practices and Product Liability Litigation*, Case No. M:05-v-01699-CRB, MDL No. 1699 ("Celebrex® and Bextra® MDL") and in its pursuit of documents properly subpoenaed from the American Medical Association ("AMA") and its publications the Journal of the American Medical Association ("JAMA") and the Archives of Internal Medicine ("AIM") (collectively, the "Journals").

2. Pfizer served subpoenas on the Journals for four categories of documents critical to its defense in the Celebrex® and Bextra® MDL: (1) "all documents . . . concerning Bextra® or Celebrex®"; (2) documents related to the "decision to publish or not publish" such manuscripts; (3) documents "regarding the peer review process or other assessment, analysis or evaluation" of such manuscripts; and (4) documents that "identify or constitute the names, affiliations and/or

comments of each person who engaged in the peer review or other assessment, analysis or evaluation" of such manuscripts. *See* Exs. B and C. Though not an exhaustive list, the subpoenas also identified five articles published in AIM and six articles published in JAMA of particular interest to Pfizer. *See id.* The return date on the subpoenas was June 11, 2007. *Id.*

3. On June 7, 2007, counsel for the Journals contacted counsel for Pfizer, objected orally to the subpoenas based on privilege, and refused to produce any documents in response to the subpoenas. *See* Ex. E. Since then, counsel for Pfizer and counsel for the Journals have engaged in numerous telephone conferences, e-mail exchanges, and letter correspondences, including at least six telephone conferences, four letters, and six e-mails from Pfizer explaining why the documents are relevant, why the privileges claimed do not apply, and why the Journals are obliged to produce the documents.

4. In August 2007, Pfizer persuaded the Journals to at least produce those documents over which the Journals were not claiming any privilege, while the parties continued to negotiate the privilege issues. *See* Ex. E.

5. On September 7, 2007, the Journals sent Pfizer a letter that lists the privileges the Journals are claiming but that does not describe the nature of the documents withheld. The Journals claim privileges under the Illinois Reporter's Privilege Act and the Illinois Medical Studies Act, and also invoke the "peer review privilege" and the "self-critical analysis" privilege. *See* Ex. E.

6. On September 14, 2007, the Journals produced what they considered to be "non-privileged" documents. The production consisted of reprints of published articles. The Journals failed to produce a privilege log or any further description of the documents withheld. *See* Ex. F.

7. On September 21, 2007, Pfizer explained why the privileges listed in the Journals' September 14, 2007 letter do not apply to the subpoenaed documents and supplied points and authority in support. *See* Ex. G. Further, cognizant of the Journals' confidentiality concerns, Pfizer emphasized its interest in information, not names, thus suggesting that the Journals redact identifying information. *See id.* Pfizer also reminded the Journals of their obligation to produce a privilege log in accordance with Rule 45(d)(2)(A). *See id.*

8. On October 25, 2007, Pfizer and the Journals spoke again. *See* Ex. H. The Journals claimed a privilege log was an unnecessary expense, claimed that Pfizer could get the information elsewhere (which it cannot) and demanded that Pfizer prove why the documents were relevant (which it already has). The Journals' position is based, in part, on the mistaken belief that Pfizer was "asking [them] to waive or violate [their] asserted privileges, so that [Pfizer] might learn the identities of peer reviewers to articles that may have been submitted but rejected . . ." (contrary to Pfizer's offer to accept redacted peer review documents, which it made a month earlier). *See* Exs. H, G.

9. On November 14, 2007, Pfizer again urged the Journals to produce a privilege log in accordance with Federal Rule of Civil Procedure 45, noting that assertions embedded in correspondence are not a valid proxy. *See* Ex. I. Pfizer urged compliance with the subpoenas, which were served more than seven months ago, and indicated its intent to file a motion to compel if the Journals refused. *See id.*

10. On January 3, 2008, counsel spoke again in the hopes of resolving this discovery dispute. The Journals' counsel indicated a willingness to accept Pfizer's proposal that they produce redacted documents in exchange for Pfizer's promise not to pursue the identity of the

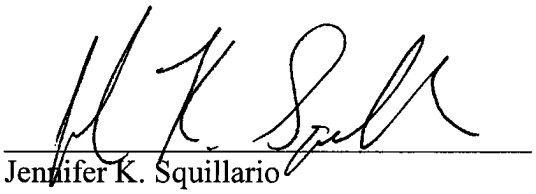
peer-reviewers. In a telephone conversation the next day, the Journals' counsel indicated the proposed compromise awaited the Journals' final approval.

11. Pfizer hoped to confirm the proposed compromise during a telephone conversation on January 10, 2008, but was disappointed to learn that the Journals changed positions and would not even agree to produce redacted documents. Pfizer then informed the Journals that it would file an appropriate motion the following week. With that, Pfizer and the Journals reached an impasse. The Journals confirmed the same in a letter dated January 11, 2008 and, via e-mail, the Journals agreed to accept service of Pfizer's motion. *See* Ex. J.

12. Pursuant to Local Rule 37.2 and Federal Rule of Civil Procedure 45, counsel for Pfizer certifies that after consultation through letters, electronic correspondence and good faith attempts to discuss and resolve this matter through telephone conversations with the Journals' counsel, Pfizer's attempts to reach an accord failed.

I declare under penalty of perjury under the laws of the United States that the foregoing is true and correct.

Dated: January 17, 2008



Jennifer K. Squillario

DLA Piper US LLP
The Marbury Building
6225 Smith Avenue
Baltimore, Maryland 21209
410-580-3000

Attorney for Pfizer Inc.

EXHIBIT B

AO88 (Rev. 12/06) Subpoena in a Civil Case

Issued by the

UNITED STATES DISTRICT COURT

NORTHERN DISTRICT OF ILLINOIS

SUBPOENA IN A CIVIL CASE

V.

IN RE: BEXTRA AND CELEBREX MARKETING SALES PRACTICES AND PRODUCT LIABILITY LITIGATION

Case Number:[1] M:05-CV-01699-CRB
MDL No. 1699
Pending in Northern District of California, San Francisco Division

TO: Archives of Internal Medicine, through the Registered Agent of Process for the American Medical Association, Jon N. Ekdahl, 515 N. State Street, Suite 14390, Chicago, IL 60610

☐ YOU ARE COMMANDED to appear in the United States District court at the place, date, and time specified below to testify in the above case.

PLACE OF TESTIMONY	COURTROOM
	DATE AND TIME

☒ YOU ARE COMMANDED to appear at the place, date, and time specified below to testify at the taking of a deposition in the above case.

PLACE OF DEPOSITION	DATE AND TIME
Winston & Strawn LLP, 35 W. Wacker Drive, Chicago, IL 60601	June 11, 2007 @ 9:00 AM

☒ YOU ARE COMMANDED to produce and permit inspection and copying of the following documents or objects at the place, date, and time specified below (list documents or objects):

See attached Exhibit A.

PLACE	DATE AND TIME
Winston & Strawn LLP, 35 W. Wacker Drive, Chicago, IL 60601	June 11, 2007 @ 9:00 AM

☐ YOU ARE COMMANDED to permit inspection of the following premises at the date and time specified below.

PREMISES	DATE AND TIME

Any organization not a party to this suit that is subpoenaed for the taking of a deposition shall designate one or more officers, directors, or managing agents, or other persons who consent to testify on its behalf, and may set forth, for each person designated, the matters on which the person will testify. Federal Rules of Civil Procedure, 30(b)(6).

ISSUING OFFICER'S SIGNATURE AND TITLE (INDICATE IF ATTORNEY FOR PLAINTIFF OR DEFENDANT)	DATE
Matthew J. Sullivan	5/7/2007

ISSUING OFFICER'S NAME, ADDRESS AND PHONE NUMBER

Matthew J. Sullivan, Winston & Strawn LLP, 35 W. Wacker Drive, Chicago, IL 60601, (312) 558-5719

(See Rule 45, Federal Rules of Civil Procedure, Subdivisions (c), (d), and (e), on next page)

[1] If action is pending in district other than district of issuance, state district under case number.

AO88 (Rev. 12/06) Subpoena in a Civil Case

PROOF OF SERVICE

DATE PLACE

SERVED

SERVED ON (PRINT NAME) MANNER OF SERVICE

SERVED BY (PRINT NAME) TITLE

DECLARATION OF SERVER

I declare under penalty of perjury under the laws of the United States of America that the foregoing information contained in the Proof of Service is true and correct.

Executed on _____
DATE

SIGNATURE OF SERVER

ADDRESS OF SERVER

Rule 45, Federal Rules of Civil Procedure, Subdivisions (c), (d), and (e), as amended on December 1, 2006:

(c) PROTECTION OF PERSONS SUBJECT TO SUBPOENAS.

(1) A party or an attorney responsible for the issuance and service of a subpoena shall take reasonable steps to avoid imposing undue burden or expense on a person subject to that subpoena. The court on behalf of which the subpoena was issued shall enforce this duty and impose upon the party or attorney in breach of this duty an appropriate sanction, which may include, but is not limited to, lost earnings and a reasonable attorney's fee.

(2) (A) A person commanded to produce and permit inspection, copying, testing, or sampling of designated electronically stored information, books, papers, documents or tangible things, or inspection of premises need not appear in person at the place of production or inspection unless commanded to appear for deposition, hearing or trial.

(B) Subject to paragraph (d)(2) of this rule, a person commanded to produce and permit inspection, copying, testing, or sampling may, within 14 days after service of the subpoena or before the time specified for compliance if such time is less than 14 days after service, serve upon the party or attorney designated in the subpoena written objection to producing any or all of the designated materials or inspection of the premises — or to producing electronically stored information in the form or forms requested. If objection is made, the party serving the subpoena shall not be entitled to inspect, copy, test, or sample the materials or inspect the premises except pursuant to an order of the court by which the subpoena was issued. If objection has been made, the party serving the subpoena may, upon notice to the person commanded to produce, move at any time for an order to compel the production, inspection, copying, testing, or sampling. Such an order to compel shall protect any person who is not a party or an officer of a party from significant expense resulting from the inspection, copying, testing, or sampling commanded.

(3) (A) On timely motion, the court by which a subpoena was issued shall quash or modify the subpoena if it

(i) fails to allow reasonable time for compliance;

(ii) requires a person who is not a party or an officer of a party to travel to a place more than 100 miles from the place where that person resides, is employed or regularly transacts business in person, except that, subject to the provisions of clause (c)(3)(B)(iii) of this rule, such a person may in order to attend trial be commanded to travel from any such place within the state in which the trial is held;

(iii) requires disclosure of privileged or other protected matter and no exception or waiver applies; or

(iv) subjects a person to undue burden.

(B) If a subpoena

(i) requires disclosure of a trade secret or other confidential research, development, or commercial information, or

(ii) requires disclosure of an unretained expert's opinion or information not describing specific events or occurrences in dispute and resulting from the expert's study made not at the request of any party, or

(iii) requires a person who is not a party or an officer of a party to incur substantial expense to travel more than 100 miles to attend trial, the court may, to protect a person subject to or affected by the subpoena, quash or modify the subpoena or, if the party in whose behalf the subpoena is issued shows a substantial need for the testimony or material that cannot be otherwise met without undue hardship and assures that the person to whom the subpoena is addressed will be reasonably compensated, the court may order appearance or production only upon specified conditions.

(d) DUTIES IN RESPONDING TO SUBPOENA.

(1) (A) A person responding to a subpoena to produce documents shall produce them as they are kept in the usual course of business or shall organize and label them to correspond with the categories in the demand.

(B) If a subpoena does not specify the form or forms for producing electronically stored information, a person responding to a subpoena must produce the information in a form or forms in which the person ordinarily maintains it or in a form or forms that are reasonably usable.

(C) A person responding to a subpoena need not produce the same electronically stored information in more than one form.

(D) A person responding to a subpoena need not provide discovery of electronically stored information from sources that the person identifies as not reasonably accessible because of undue burden or cost. On motion to compel discovery or to quash, the person from whom discovery is sought must show that the information sought is not reasonably accessible because of undue burden or cost. If that showing is made, the court may nonetheless order discovery from such sources if the requesting party shows good cause, considering the limitations of Rule 26(b)(2)(C). The court may specify conditions for the discovery.

(2) (A) When information subject to a subpoena is withheld on a claim that it is privileged or subject to protection as trial-preparation materials, the claim shall be made expressly and shall be supported by a description of the nature of the documents, communications, or things not produced that is sufficient to enable the demanding party to contest the claim.

(B) If information is produced in response to a subpoena that is subject to a claim of privilege or of protection as trial-preparation material, the person making the claim may notify any party that received the information of the claim and the basis for it. After being notified, a party must promptly return, sequester, or destroy the specified information and any copies it has and may not use or disclose the information until the claim is resolved. A receiving party may promptly present the information to the court under seal for a determination of the claim. If the receiving party disclosed the information before being notified, it must take reasonable steps to retrieve it. The person who produced the information must preserve the information until the claim is resolved.

(e) CONTEMPT. Failure of any person without adequate excuse to obey a subpoena served upon that person may be deemed a contempt of the court from which the subpoena issued. An adequate cause for failure to obey exists when a subpoena purports to require a nonparty to attend or produce at a place not within the limits provided by clause (ii) of subparagraph (c)(3)(A).

EXHIBIT A

INSTRUCTIONS

1. Each Request requires the *Archives of Internal Medicine* to produce all documents requested herein that were created by, or that came into the possession, custody or control of the *Archives of Internal Medicine*, or any of its affiliates, predecessors or successors, from all files or other sources that contain responsive documents, wherever located and whether active, in storage or otherwise.

2. Unless otherwise specified, the Requests below are requested for the period from January 1, 1998 through and including the present.

3. Where only a portion of a document contains information responsive to the Requests below, produce the entire document along with all attachments, appendices and exhibits.

4. If any document is withheld from production on the basis of a claim of privilege or otherwise, identify each document and the grounds upon which its production is being withheld.

5. All documents shall be produced by you as they are kept in the usual course of business with any identifying labels, file markings, or similar identifying features. If there are no documents responsive to a category specified below, you shall so state in a writing produced at the time and place that documents are demanded by these Requests.

6. If any document is unavailable because it was lost or destroyed by the *Archives of Internal Medicine* or its agents, identify each document, the person who destroyed the document or who authorized its destruction, and each person who has knowledge of the document.

7. These Requests shall be deemed continuing, to the full extent required or permitted under the Federal Rules of Civil Procedure, so as to require supplementary production when the *Archives of Internal Medicine* or its agents obtain access, custody, possession or control of any document not previously produced which is responsive to any of these Requests.

DEFINITIONS

1. The words "you," "yours" and/or "yourselves" means the *Archives of Internal Medicine* and any of your agents, representatives or assigns, or other persons acting, or purporting to act, on your behalf.

2. "Document" means all written or graphic material or any other means of preserving thought or expression of every type and description, regardless of origin or location, whether written, recorded, transcribed, taped, punched, filmed, microfilmed, or in any other way produced, reproduced or recorded, including, without limitation, originals, drafts, computer-sorted and computer-retrievable information, copies or duplicates that

are marked with any notation or annotation, copies or duplicates that differ in any way from the original, correspondence, memoranda, reports, notes, minutes, contracts, agreements, books, records, checks, vouchers, invoices, calendars, appointment books, purchase orders, ledgers, diaries, logs, calendar notes, computer printouts, computer disks, card files, lists of persons attending meetings or conferences, sketches, diagrams, calculations, evaluations, analyses, directions, work papers, press clippings, sworn or unsworn statements of employees, requisitions, manuals or guidelines, audit work papers, financial analyses, tables of organizations, charts, graphs, indices, advertisements or other promotional materials, audited and unaudited financial statements, trade letters, trade publications, newspapers or newsletters, photographs, e-mail, electronic or mechanical records, telegrams, telecopies, audiotapes, and all other receptacles or repositories housing or containing such documents, and all other media used to record, in any form, information. "Document" expressly includes all "Electronically Stored Information."

3. "Electronically Stored Information" means all writings, drawings, graphs, charts, photographs, sound recordings, images, and other data or data compilations stored in any medium from which information can be obtained. "Electronically Stored Information" includes, by way of example and not limitation, computer programs (whether private, commercial or work-in-progress), programming notes or instructions, activity listings of electronic mail recipients and/or transmittals, output resulting from the use of any software program, including word processing documents, spreadsheets, database files, charts, graphs and outlines, electronic mail, and any and all miscellaneous files and/or file fragments, regardless of the media on which they reside and regardless of whether said Electronically Stored Information exists in an active file, deleted file or file fragment. "Electronically Stored Information" also includes but is not limited to any and all items stored on computer memories, hard disks, diskettes and cartridges, network drives, network memory storage, archived tapes and cartridges, magnetic tapes of all types, microfiches and any other vehicle used for digital data storage and/or transmittal.

4. "Agent" means any agent, employee, officer, director, attorney, independent contractor or any other person acting at the direction of or on behalf of another.

5. The word "person(s)" as used in this Request is defined as any natural person or any business, legal or governmental entity or association.

6. The term "concerning" means relating to, referring to, describing, evidencing, constituting, embodying, comprising, reflecting, identifying, commenting on, responding to, analyzing, or containing factual or opinion information on a subject or in any other way directly or indirectly pertaining to that subject.

7. The following rules of construction apply:
   a. The use of the singular form of any word includes the plural and vice versa.
   b. The connectives "and" and "or" shall be construed either disjunctively or conjunctively as necessary to bring within the scope of the discovery request all responses that might otherwise be construed to be outside of its scope.

SCHEDULE OF DOCUMENTS & OTHER THINGS TO BE PRODUCED

1. All documents regarding manuscripts submitted for publication to the *Archives of Internal Medicine*, whether accepted or rejected, concerning Bextra or Celebrex, including but not limited to:

   a. James R. Sowers, MD et al., *The Effects of Cyclooxygenase-2 Inhibitors and Nonsteroidal Anti-Inflammatory Therapy on 24-Hour Blood Pressure in Patients With Hypertension, Osteoarthritis, and Type 2 Diabetes Mellitus*, 165 ARCH. INTERN. MED. 161-68 (2005).
   b. Muhammad Mamdani, PharmD, MA, MPH et al., *Effect of Selective Cyclooxygenase 2 Inhibitors and Naproxen on Short-term Risk of Acute Myocardial Infarction in the Elderly*, 163 ARCH. INTERN. MED. 481-86 (2003).
   c. Daniel H. Solomon, MD, MPH et al., *Nonsteroidal Anti-inflammatory Drug Use and Acute Myocardial Infarction*, 162 ARCH. INTERN. MED. 1099-1104 (2002).
   d. Soren P. Johnsen, MD, PhD et al., *Risk of Hospitalization for Myocardial Infarction Among Users of Rofecoxib, Celecoxib, and Other NSAIDs*, 165 ARCH. INTERN. MED. 978-84 (2005).
   e. T.J. Aw et al., *Meta-analysis of Cyclooxygenase-2 Inhibitors and Their Effects on Blood Pressure*, 165 ARCH. INTERN. MED. 490-6 (2005).

2. All documents regarding the decision to publish or not publish any manuscripts submitted for publication to the *Archives of Internal Medicine*, whether accepted or rejected, concerning Bextra or Celebrex, including but not limited to:

   a. James R. Sowers, MD et al., *The Effects of Cyclooxygenase-2 Inhibitors and Nonsteroidal Anti-Inflammatory Therapy on 24-Hour Blood Pressure in Patients With Hypertension, Osteoarthritis, and Type 2 Diabetes Mellitus*, 165 ARCH. INTERN. MED. 161-68 (2005).
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   d. Soren P. Johnsen, MD, PhD et al., *Risk of Hospitalization for Myocardial Infarction Among Users of Rofecoxib, Celecoxib, and Other NSAIDs*, 165 ARCH. INTERN. MED. 978-84 (2005).
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3. All documents regarding the peer review process or other assessment, analysis or evaluation of any manuscripts submitted for publication to the *Archives of Internal Medicine*, whether accepted or rejected, concerning Bextra or Celebrex, including but not limited to:

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   e. T.J. Aw et al., *Meta-analysis of Cyclooxygenase-2 Inhibitors and Their Effects on Blood Pressure*, 165 ARCH. INTERN. MED. 490-6 (2005).

4. All documents which identify or constitute the names, affiliations and/or comments of each person who engaged in the peer review or other assessment, analysis or evaluation of any manuscripts submitted for publication to the *Archives of Internal Medicine*, whether accepted or rejected, concerning Bextra or Celebrex, including but not limited to:

   a. James R. Sowers, MD et al., *The Effects of Cyclooxygenase-2 Inhibitors and Nonsteroidal Anti-Inflammatory Therapy on 24-Hour Blood Pressure in Patients With Hypertension, Osteoarthritis, and Type 2 Diabetes Mellitus*, 165 ARCH. INTERN. MED. 161-68 (2005).
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   e. T.J. Aw et al., *Meta-analysis of Cyclooxygenase-2 Inhibitors and Their Effects on Blood Pressure*, 165 ARCH. INTERN. MED. 490-6 (2005).

AMY W. SCHULMAN
DLA PIPER US LLP
1251 Avenue of the Americas, 29th Floor
New York, NY 10020-1104
Tel: 212.335.4500
Fax: 212.335.4501
amy.schulman@dlapiper.com

Defendants' Liaison Counsel

UNITED STATES DISTRICT COURT

NORTHERN DISTRICT OF CALIFORNIA

SAN FRANCISCO DIVISION

IN RE: BEXTRA AND CELEBREX MARKETING SALES PRACTICES AND PRODUCT LIABILITY LITIGATION	CASE NO. M:05-CV-01699-CRB MDL No. 1699
This Pleading Relates to: ALL CASES.	**NOTICE OF ISSUANCE OF SUBPOENAS**

PLEASE TAKE NOTICE that pursuant to Federal Rules of Civil Procedure 30 and 45, Defendants Pfizer Inc., Pharmacia Corporation, and G.D. Searle, LLC, through undersigned counsel, have issued the subpoenas attached hereto as Exhibits A and B for the depositions of, and the production of documents and other things by, the *Archives of Internal Medicine* and the *Journal of the American Medical Association.*

Dated: June 8, 2007

DLA PIPER US LLP

By /s/
AMY W. SCHULMAN
Defendants' Liaison Counsel

EXHIBIT C

AO88 (Rev. 12/06) Subpoena in a Civil Case

Issued by the

UNITED STATES DISTRICT COURT

NORTHERN DISTRICT OF ILLINOIS

SUBPOENA IN A CIVIL CASE

V.

IN RE: BEXTRA AND CELEBREX MARKETING SALES PRACTICES AND PRODUCT LIABILITY LITIGATION

Case Number:[1] M:05-CV-01699-CRB
MDL No. 1699
Pending in Northern District of California, San Francisco Division

TO: Journal of the American Medical Association, through the Registered Agent of Process for the American Medical Association, Jon N. Ekdahl, 515 N. State Street, Suite 14390, Chicago, IL 60610

☐ YOU ARE COMMANDED to appear in the United States District court at the place, date, and time specified below to testify in the above case.

PLACE OF TESTIMONY	COURTROOM
	DATE AND TIME

☒ YOU ARE COMMANDED to appear at the place, date, and time specified below to testify at the taking of a deposition in the above case.

PLACE OF DEPOSITION	DATE AND TIME
Winston & Strawn LLP, 35 W. Wacker Drive, Chicago, IL 60601	June 11, 2007 @ 9:00 AM

☒ YOU ARE COMMANDED to produce and permit inspection and copying of the following documents or objects at the place, date, and time specified below (list documents or objects):

See attached Exhibit A.

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Any organization not a party to this suit that is subpoenaed for the taking of a deposition shall designate one or more officers, directors, or managing agents, or other persons who consent to testify on its behalf, and may set forth, for each person designated, the matters on which the person will testify. Federal Rules of Civil Procedure, 30(b)(6).

ISSUING OFFICER'S SIGNATURE AND TITLE (INDICATE IF ATTORNEY FOR PLAINTIFF OR DEFENDANT)	DATE
Matthew J. Sullivan	5/7/2007

ISSUING OFFICER'S NAME, ADDRESS AND PHONE NUMBER

Matthew J. Sullivan, Winston & Strawn LLP, 35 W. Wacker Drive, Chicago, IL 60601, (312) 558-5719

(See Rule 45, Federal Rules of Civil Procedure, Subdivisions (c), (d), and (e), on next page)

[1] If action is pending in district other than district of issuance, state district under case number.

AO88 (Rev. 12/06) Subpoena in a Civil Case

PROOF OF SERVICE

DATE PLACE

SERVED

SERVED ON (PRINT NAME) MANNER OF SERVICE

SERVED BY (PRINT NAME) TITLE

DECLARATION OF SERVER

I declare under penalty of perjury under the laws of the United States of America that the foregoing information contained in the Proof of Service is true and correct.

Executed on _____
DATE

SIGNATURE OF SERVER

ADDRESS OF SERVER

Rule 45, Federal Rules of Civil Procedure, Subdivisions (c), (d), and (e), as amended on December 1, 2006:

(c) PROTECTION OF PERSONS SUBJECT TO SUBPOENAS.

(1) A party or an attorney responsible for the issuance and service of a subpoena shall take reasonable steps to avoid imposing undue burden or expense on a person subject to that subpoena. The court on behalf of which the subpoena was issued shall enforce this duty and impose upon the party or attorney in breach of this duty an appropriate sanction, which may include, but is not limited to, lost earnings and a reasonable attorney's fee.

(2) (A) A person commanded to produce and permit inspection, copying, testing, or sampling of designated electronically stored information, books, papers, documents or tangible things, or inspection of premises need not appear in person at the place of production or inspection unless commanded to appear for deposition, hearing or trial.

(B) Subject to paragraph (d)(2) of this rule, a person commanded to produce and permit inspection, copying, testing, or sampling may, within 14 days after service of the subpoena or before the time specified for compliance if such time is less than 14 days after service, serve upon the party or attorney designated in the subpoena written objection to producing any or all of the designated materials or inspection of the premises — or to producing electronically stored information in the form or forms requested. If objection is made, the party serving the subpoena shall not be entitled to inspect, copy, test, or sample the materials or inspect the premises except pursuant to an order of the court by which the subpoena was issued. If objection has been made, the party serving the subpoena may, upon notice to the person commanded to produce, move at any time for an order to compel the production, inspection, copying, testing, or sampling. Such an order to compel shall protect any person who is not a party or an officer of a party from significant expense resulting from the inspection, copying, testing, or sampling commanded.

(3) (A) On timely motion, the court by which a subpoena was issued shall quash or modify the subpoena if it

(i) fails to allow reasonable time for compliance;

(ii) requires a person who is not a party or an officer of a party to travel to a place more than 100 miles from the place where that person resides, is employed or regularly transacts business in person, except that, subject to the provisions of clause (c)(3)(B)(iii) of this rule, such a person may in order to attend trial be commanded to travel from any such place within the state in which the trial is held;

(iii) requires disclosure of privileged or other protected matter and no exception or waiver applies; or

(iv) subjects a person to undue burden.

(B) If a subpoena

(i) requires disclosure of a trade secret or other confidential research, development, or commercial information, or

(ii) requires disclosure of an unretained expert's opinion or information not describing specific events or occurrences in dispute and resulting from the expert's study made not at the request of any party, or

(iii) requires a person who is not a party or an officer of a party to incur substantial expense to travel more than 100 miles to attend trial, the court may, to protect a person subject to or affected by the subpoena, quash or modify the subpoena or, if the party in whose behalf the subpoena is issued shows a substantial need for the testimony or material that cannot be otherwise met without undue hardship and assures that the person to whom the subpoena is addressed will be reasonably compensated, the court may order appearance or production only upon specified conditions.

(d) DUTIES IN RESPONDING TO SUBPOENA.

(1) (A) A person responding to a subpoena to produce documents shall produce them as they are kept in the usual course of business or shall organize and label them to correspond with the categories in the demand.

(B) If a subpoena does not specify the form or forms for producing electronically stored information, a person responding to a subpoena must produce the information in a form or forms in which the person ordinarily maintains it or in a form or forms that are reasonably usable.

(C) A person responding to a subpoena need not produce the same electronically stored information in more than one form.

(D) A person responding to a subpoena need not provide discovery of electronically stored information from sources that the person identifies as not reasonably accessible because of undue burden or cost. On motion to compel discovery or to quash, the person from whom discovery is sought must show that the information sought is not reasonably accessible because of undue burden or cost. If that showing is made, the court may nonetheless order discovery from such sources if the requesting party shows good cause, considering the limitations of Rule 26(b)(2)(C). The court may specify conditions for the discovery.

(2) (A) When information subject to a subpoena is withheld on a claim that it is privileged or subject to protection as trial-preparation materials, the claim shall be made expressly and shall be supported by a description of the nature of the documents, communications, or things not produced that is sufficient to enable the demanding party to contest the claim.

(B) If information is produced in response to a subpoena that is subject to a claim of privilege or of protection as trial-preparation material, the person making the claim may notify any party that received the information of the claim and the basis for it. After being notified, a party must promptly return, sequester, or destroy the specified information and any copies it has and may not use or disclose the information until the claim is resolved. A receiving party may promptly present the information to the court under seal for a determination of the claim. If the receiving party disclosed the information before being notified, it must take reasonable steps to retrieve it. The person who produced the information must preserve the information until the claim is resolved.

(e) CONTEMPT. Failure of any person without adequate excuse to obey a subpoena served upon that person may be deemed a contempt of the court from which the subpoena issued. An adequate cause for failure to obey exists when a subpoena purports to require a nonparty to attend or produce at a place not within the limits provided by clause (ii) of subparagraph (c)(3)(A).

EXHIBIT A

INSTRUCTIONS

1. Each Request requires the *Journal of the American Medical Association* to produce all documents requested herein that were created by, or that came into the possession, custody or control of the *Journal of the American Medical Association*, or any of its affiliates, predecessors or successors, from all files or other sources that contain responsive documents, wherever located and whether active, in storage or otherwise.

2. Unless otherwise specified, the Requests below are requested for the period from January 1, 1998 through and including the present.

3. Where only a portion of a document contains information responsive to the Requests below, produce the entire document along with all attachments, appendices and exhibits.

4. If any document is withheld from production on the basis of a claim of privilege or otherwise, identify each document and the grounds upon which its production is being withheld.

5. All documents shall be produced by you as they are kept in the usual course of business with any identifying labels, file markings, or similar identifying features. If there are no documents responsive to a category specified below, you shall so state in a writing produced at the time and place that documents are demanded by these Requests.

6. If any document is unavailable because it was lost or destroyed by the *Journal of the American Medical Association* or its agents, identify each document, the person who destroyed the document or who authorized its destruction, and each person who has knowledge of the document.

7. These Requests shall be deemed continuing, to the full extent required or permitted under the Federal Rules of Civil Procedure, so as to require supplementary production when the *Journal of the American Medical Association* or its agents obtain access, custody, possession or control of any document not previously produced which is responsive to any of these Requests.

DEFINITIONS

1. The words "you," "yours" and/or "yourselves" means the *Journal of the American Medical Association* and any of your agents, representatives or assigns, or other persons acting, or purporting to act, on your behalf.

2. "Document" means all written or graphic material or any other means of preserving thought or expression of every type and description, regardless of origin or location, whether written, recorded, transcribed, taped, punched, filmed, microfilmed, or in any other way produced, reproduced or recorded, including, without limitation, originals,

drafts, computer-sorted and computer-retrievable information, copies or duplicates that are marked with any notation or annotation, copies or duplicates that differ in any way from the original, correspondence, memoranda, reports, notes, minutes, contracts, agreements, books, records, checks, vouchers, invoices, calendars, appointment books, purchase orders, ledgers, diaries, logs, calendar notes, computer printouts, computer disks, card files, lists of persons attending meetings or conferences, sketches, diagrams, calculations, evaluations, analyses, directions, work papers, press clippings, sworn or unsworn statements of employees, requisitions, manuals or guidelines, audit work papers, financial analyses, tables of organizations, charts, graphs, indices, advertisements or other promotional materials, audited and unaudited financial statements, trade letters, trade publications, newspapers or newsletters, photographs, e-mail, electronic or mechanical records, telegrams, telecopies, audiotapes, and all other receptacles or repositories housing or containing such documents, and all other media used to record, in any form, information. "Document" expressly includes all "Electronically Stored Information."

3. "Electronically Stored Information" means all writings, drawings, graphs, charts, photographs, sound recordings, images, and other data or data compilations stored in any medium from which information can be obtained. "Electronically Stored Information" includes, by way of example and not limitation, computer programs (whether private, commercial or work-in-progress), programming notes or instructions, activity listings of electronic mail recipients and/or transmittals, output resulting from the use of any software program, including word processing documents, spreadsheets, database files, charts, graphs and outlines, electronic mail, and any and all miscellaneous files and/or file fragments, regardless of the media on which they reside and regardless of whether said Electronically Stored Information exists in an active file, deleted file or file fragment. "Electronically Stored Information" also includes but is not limited to any and all items stored on computer memories, hard disks, diskettes and cartridges, network drives, network memory storage, archived tapes and cartridges, magnetic tapes of all types, microfiches and any other vehicle used for digital data storage and/or transmittal.

4. "Agent" means any agent, employee, officer, director, attorney, independent contractor or any other person acting at the direction of or on behalf of another.

5. The word "person(s)" as used in this Request is defined as any natural person or any business, legal or governmental entity or association.

6. The term "concerning" means relating to, referring to, describing, evidencing, constituting, embodying, comprising, reflecting, identifying, commenting on, responding to, analyzing, or containing factual or opinion information on a subject or in any other way directly or indirectly pertaining to that subject.

7. The following rules of construction apply:
   a. The use of the singular form of any word includes the plural and vice versa.
   b. The connectives "and" and "or" shall be construed either disjunctively or conjunctively as necessary to bring within the scope of the discovery request all responses that might otherwise be construed to be outside of its scope.

SCHEDULE OF DOCUMENTS & OTHER THINGS TO BE PRODUCED

1. All documents regarding manuscripts submitted for publication to the *Journal of the American Medical Association*, whether accepted or rejected, concerning Bextra or Celebrex, including but not limited to:

   a. Debabrata Mukherjee, MD et al., *Risk of Cardiovascular Events Associated With Selective COX-2 Inhibitors*, 286 JAMA 954-59 (2001).
   b. Fred E. Silverstein, MD et al., *Gastrointestinal Toxicity With Celecoxib vs Nonsteroidal Anti-inflammatory Drugs for Osteoarthritis and Rheumatoid Arthritis: The CLASS Study: A Randomized Controlled Trial*, 284 JAMA 1247-55 (2000).
   c. Patricia McGettigan, MD, FRACP & David Henry, MB, ChB, FRCP, *Cardiovascular Risk and Inhibition of Cyclooxygenase: A Systematic Review of the Observational Studies of Selective and Nonselective Inhibitors of Cyclooxygenase 2*, 296 JAMA 1633-44 (2006).
   d. David J. Graham, MD, MPH, *COX-2 Inhibitors, Other NSAIDs, and Cardiovascular Risk: The Seduction of Common Sense*, 296 JAMA 1653-56 (2006).
   e. Lee Simon et al., *CLASS: The Celecoxib Long Term Arthritis Safety Study: An Assessment of Analytical Methods* (rejected 2004).
   f. *Analgesic Efficacy and Safety of Parecoxib Sodium, A New Intravenous COX-2 Inhibitor, In Patients Undergoing Coronary Artery Bypass Grafting* (rejected 2002).

2. All documents regarding the decision to publish or not publish any manuscripts submitted for publication to the *Journal of the American Medical Association*, whether accepted or rejected, concerning Bextra or Celebrex, including but not limited to:

   a. Debabrata Mukherjee, MD et al., *Risk of Cardiovascular Events Associated With Selective COX-2 Inhibitors*, 286 JAMA 954-59 (2001).
   b. Fred E. Silverstein, MD et al., *Gastrointestinal Toxicity With Celecoxib vs Nonsteroidal Anti-inflammatory Drugs for Osteoarthritis and Rheumatoid Arthritis: The CLASS Study: A Randomized Controlled Trial*, 284 JAMA 1247-55 (2000).
   c. Patricia McGettigan, MD, FRACP & David Henry, MB, ChB, FRCP, *Cardiovascular Risk and Inhibition of Cyclooxygenase: A Systematic Review of the Observational Studies of Selective and Nonselective Inhibitors of Cyclooxygenase 2*, 296 JAMA 1633-44 (2006).
   d. David J. Graham, MD, MPH, *COX-2 Inhibitors, Other NSAIDs, and Cardiovascular Risk: The Seduction of Common Sense*, 296 JAMA 1653-56 (2006).
   e. Lee Simon et al., *CLASS: The Celecoxib Long Term Arthritis Safety Study: An Assessment of Analytical Methods* (rejected 2004).

f. *Analgesic Efficacy and Safety of Parecoxib Sodium, A New Intravenous COX-2 Inhibitor, In Patients Undergoing Coronary Artery Bypass Grafting* (rejected 2002).

3. All documents regarding the peer review process or other assessment, analysis or evaluation of any manuscripts submitted for publication to the *Journal of the American Medical Association*, whether accepted or rejected, concerning Bextra or Celebrex, including but not limited to:

a. Debabrata Mukherjee, MD et al., *Risk of Cardiovascular Events Associated With Selective COX-2 Inhibitors*, 286 JAMA 954-59 (2001).
b. Fred E. Silverstein, MD et al., *Gastrointestinal Toxicity With Celecoxib vs Nonsteroidal Anti-inflammatory Drugs for Osteoarthritis and Rheumatoid Arthritis: The CLASS Study: A Randomized Controlled Trial*, 284 JAMA 1247-55 (2000).
c. Patricia McGettigan, MD, FRACP & David Henry, MB, ChB, FRCP, *Cardiovascular Risk and Inhibition of Cyclooxygenase: A Systematic Review of the Observational Studies of Selective and Nonselective Inhibitors of Cyclooxygenase 2*, 296 JAMA 1633-44 (2006).
d. David J. Graham, MD, MPH, *COX-2 Inhibitors, Other NSAIDs, and Cardiovascular Risk: The Seduction of Common Sense*, 296 JAMA 1653-56 (2006).
e. Lee Simon et al., *CLASS: The Celecoxib Long Term Arthritis Safety Study: An Assessment of Analytical Methods* (rejected 2004).
f. *Analgesic Efficacy and Safety of Parecoxib Sodium, A New Intravenous COX-2 Inhibitor, In Patients Undergoing Coronary Artery Bypass Grafting* (rejected 2002).

4. All documents which identify or constitute the names, affiliations and/or comments of each person who engaged in the peer review or other assessment, analysis or evaluation of any manuscripts submitted for publication to the *Journal of the American Medical Association*, whether accepted or rejected, concerning Bextra or Celebrex, including but not limited to:

a. Debabrata Mukherjee, MD et al., *Risk of Cardiovascular Events Associated With Selective COX-2 Inhibitors*, 286 JAMA 954-59 (2001).
b. Fred E. Silverstein, MD et al., *Gastrointestinal Toxicity With Celecoxib vs Nonsteroidal Anti-inflammatory Drugs for Osteoarthritis and Rheumatoid Arthritis: The CLASS Study: A Randomized Controlled Trial*, 284 JAMA 1247-55 (2000).
c. Patricia McGettigan, MD, FRACP & David Henry, MB, ChB, FRCP, *Cardiovascular Risk and Inhibition of Cyclooxygenase: A Systematic Review of the Observational Studies of Selective and Nonselective Inhibitors of Cyclooxygenase 2*, 296 JAMA 1633-44 (2006).

d. David J. Graham, MD, MPH, *COX-2 Inhibitors, Other NSAIDs, and Cardiovascular Risk: The Seduction of Common Sense*, 296 JAMA 1653-56 (2006).

e. Lee Simon et al., *CLASS: The Celecoxib Long Term Arthritis Safety Study: An Assessment of Analytical Methods* (rejected 2004).

f. *Analgesic Efficacy and Safety of Parecoxib Sodium, A New Intravenous COX-2 Inhibitor, In Patients Undergoing Coronary Artery Bypass Grafting* (rejected 2002).

EXHIBIT D

UNITED STATES DISTRICT COURT

NORTHERN DISTRICT OF CALIFORNIA

IN RE: BEXTRA AND CELEBREX MARKETING SALES PRACTICES AND PRODUCT LIABILITY LITIGATION	CASE NO. M:05-CV-01699-CRB MDL No. 1699
This Order Relates to: ALL CASES	**MEMORANDUM AND ORDER RE: MOTIONS TO EXCLUDE EXPERT TESTIMONY**

In this Multi-District Litigation ("MDL") proceeding, over 3000 plaintiffs allege that they or their loved ones suffered a heart attack, stroke or other adverse cardiovascular event as a result of taking Celebrex, a pain medication manufactured by defendant Pfizer, Inc. ("Pfizer"). Pfizer has moved to exclude any expert testimony to the effect that Celebrex is capable of causing a heart attack or stroke when ingested at 200 milligrams a day or 400 milligrams a day. Plaintiffs have also moved to exclude certain expert testimony offered by Pfizer. The Court held three days of hearings which included direct and cross examination of certain experts. After carefully considering the parties' memoranda and evidence, and the testimony offered at the hearing, the Court concludes that plaintiffs have not presented scientifically reliable evidence that Celebrex causes heart attacks or strokes when ingested at the 200 milligram a day dose. In all other respects the parties' motions are denied.

BACKGROUND

Non-steroidal anti-inflammatory drugs ("NSAIDs") have been widely used for pain relief for several years. NSAIDs, however, have certain side effects, including gastrointestinal toxicity which results in thousands of deaths every year. The pharmaceutical company Merck & Co., Inc. ("Merck") developed Vioxx, and Pfizer (or, more precisely, its predecessors) developed Celebrex and Bextra, NSAIDs known as COX-2 inhibitors, with the expectation that they would have fewer gastrointestinal side effects than traditional NSAIDs. The Food and Drug Administration ("FDA") approved Celebrex for adult arthritis in 1998, Vioxx in 1999, and Bextra in late 2001. The recommended dose of Celebrex was and is 200 milligrams a day ("mg/d") for arthritis and 400 mg/d for rheumatoid arthritis.

In 2000 the results of a long-term randomized study of Celebrex known as CLASS ("Celecoxib Long-Term Arthritis Safety Study") were published. The study was designed to evaluate the gastrointestinal side effects of taking Celebrex at 800 mg/d. Based on investigator reported cardiovascular events, the study showed no increased risk of heart attack or stroke by taking Celebrex over diclofenac or ibuprofen. Around the same time, a similar study of Vioxx, known as VIGOR, showed a four-fold increase in cardiovascular ("cv") risk for patients taking Vioxx versus Aleve (naproxen). The FDA subsequently revised the labels of Celebrex and Vioxx to reflect the cv risk results of these studies.

Another Vioxx randomized clinical study, known as APPROVe, was published in 2004. This study demonstrated a two-fold increased risk of cv adverse events for patients taking Vioxx versus a placebo. This study contributed to Merck's voluntary removal of Vioxx from the market on September 30, 2004.

The preliminary results of APC, a randomized, placebo-controlled study of Celebrex at 200 mg twice daily (400 mg/d) and 400 mg twice daily (800 mg/d) to evaluate whether Celebrex prevents the development of colon polyps, became available in late 2004. APC showed dose-related increased cv risk for patients taking Celebrex compared to placebo: more than doubling the risk for 200 mg twice daily and tripling the risk for

400 mg twice daily. The APC steering committee discontinued the study in December 2004 because of these preliminary results.

In February 2005 the FDA convened an Advisory Committee to review the data on cv risk and NSAIDs, including COX-2 inhibitors. The Committee concluded that all COX-2 inhibitors increase cv risk versus placebo, but it did not make any findings as to what dose is required to increase the risk. It also concluded that the data was insufficient to determine if traditional NSAIDs also increase cv risk. With respect to Celebrex, the FDA found that APC is the "strongest data in support of an increased risk of serious adverse CV events." FDA Decision Memorandum, April 6, 2005, at 4, Declaration of Loren Brown ("Brown Decl.") Exh. 16. The FDA also noted that APC's results had not been replicated by preliminary data from two other randomized controlled clinical studies: (1) PreSAP, a colon polyp prevention trial of Celebrex at 400 mg/d; and (2) ADAPT, an Alzheimer's trial of Celebrex at 200 twice daily (400 mg/d). Both studies showed no increased cv risk for Celebrex versus placebo.

The FDA subsequently asked Pfizer to remove Bextra from the market, which Pfizer did in April 2005. The FDA also determined that the benefits of Celebrex outweigh its risks and therefore it allowed Celebrex to remain on the market. Celebrex is the only COX-2 inhibitor currently on the market.

The FDA also directed all NSAIDs, including Celebrex, to include a black box warning on their labels. The black box warns of cv risk as follows:

> **Cardiovascular Risk**
>
> - CELEBREX may cause an increased risk of serious cardiovascular thrombotic events, myocardial infarction, and stroke, which can be fatal. All NSAIDs may have a similar risk. This risk may increase with duration of use. Patients with cardiovascular disease or risk factors for cardiovascular disease may be at greater risk . . . .

Celebrex 2007 Label, Brown Decl. Exh. 3.

As a result of these developments, thousands of patients and patient representatives filed lawsuits against Merck and Pfizer alleging that the patient had suffered a serious

cardiovascular injury, such as a heart attack or stroke, due to their ingestion of Vioxx, and/or Celebrex and/or Bextra. All of the federal court claims against Merck were consolidated in a MDL action in New Orleans. All of the federal court claims against Pfizer were consolidated into this MDL proceeding.

THE DAUBERT MOTIONS

Pursuant to Federal Rule of Evidence 702, Pfizer moves to exclude plaintiffs' experts from offering the following six opinions:

1. That 200 mg/d of Celebrex causes heart attacks and strokes;
2. That 400 mg/d of Celebrex causes heart attacks and strokes;
3. That Celebrex causes heart attacks or strokes more than three days after a patient stops taking it;
4. That Celebrex causes strokes; and;
5. That Celebrex causes heart attacks or stokes at durations of less than 33 months of continuous daily use.

Pfizer also asks the Court to exclude any expert opinion that Celebrex caused any individual plaintiff's heart or stroke absent epidemiology evidence that demonstrates a relative risk greater than 2.0, that is, that Celebrex doubles the risk. Plaintiffs have moved to exclude certain expert testimony offered by Pfizer; specifically, they seek to exclude admission of the meta-analyses performed by plaintiffs' experts.

In connection with these motions, the parties submitted direct written testimony of their respective experts as well as legal memoranda. The Court then held three days of hearings, which were conducted jointly with the New York Justice presiding over the New York State Celebrex and Bextra cases. Plaintiffs' experts Dr. Neil Doherty, Dr. Joel Bennett, Dr. Nicholas Jewell and Dr. Maryilyn Rymer testified on direct and cross-examination, along with defendant's expert Dr. Milton Packer. The parties also submitted post-hearing memoranda. The motions are now ripe for decision.

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LEGAL STANDARD

A. Admissibility of Expert Testimony

When evaluating the admissibility of expert testimony, the trial judge "must engage in a difficult, two-part analysis." Daubert v. Merrill Dow Pharmaceuticals, Inc., 43 F.3d 1311, 1315 (9th Cir. 1995) (Daubert II). First, the court must "determine nothing less than whether the experts' testimony reflects 'scientific knowledge,' whether their findings are 'derived by the scientific method,' and whether their work product amounts to 'good science.'" Id. (quoting Daubert v. Merrell Dow Pharmaceuticals, Inc., 509 U.S. 579, 589-90, 593 (1993)); see also In Re Silicone Gel Breast Impl. Prod. Liab. Lit., 318 F.Supp.2d 879, 890 (C.D. Cal. 2004) ("'[T]he trial judge in all cases of proffered expert testimony must find that it is properly grounded, well-reasoned, and not speculative before it can be admitted.'") (quoting Fed. R. Evid. 702 Advisory Committee's Notes). The trial judge's obligation "is to make certain that an expert . . . employs in the courtroom the same level of intellectual rigor that characterizes the practice of an expert in the relevant field." Kumho Tire Co. v. Carmichael, 526 U.S. 137, 152 (1999).

Many factors may be relevant to the reliability inquiry, including: (1) whether the proffered theory or technique has been tested, (2) whether the theory or technique has been subjected to peer review and publication, (3) the known or potential rate of error of the technique or theory when applied, and (4) the "general acceptance" of the theory or technique in the scientific community. Daubert, 509 U.S. at 593-94.

> [C]ourts have also found the following factors relevant in assessing the reliability of expert testimony: (1) whether the expert is proposing to testify about matters growing directly out of independent research he or she has conducted or whether the opinion was developed expressly for purposes of testifying; (2) whether the expert has unjustifiably extrapolated from an accepted premise to an unfounded conclusion; (3) whether the expert has adequately accounted for obvious alternative explanations; (4) whether the expert is being as careful as he would be in his regular professional work; and (5) whether the field of expertise claimed by the expert is known to reach reliable results for the type of opinion offered.

In Re Silicone Gel Breast Impl. Prod. Liab. Lit., 318 F.Supp.2d at 890 (citing Fed.R.Evid. 702 Advisory Committee's Notes).

In addition to determining reliability, the court "must ensure that the proposed expert testimony is 'relevant to the task at hand,' i.e., that it logically advances a material aspect of the proposing party's case." Daubert II, 43 F.3d at 1315 (quoting Daubert, 509 U.S. at 597). This is known as the "fit" requirement. Id. Here, the pertinent fit inquiry is "causation." The parties' motions address expert testimony on the causation inquiry.

B. Causation

Causation in toxic tort or pharmaceutical personal injury cases "is typically discussed in terms of generic and specific causation." In Re Hanford Nuclear Reservation Lit., 292 F.3d 1124, 1133 (9th Cir. 2002). General or generic causation means "whether the substance at issue had the capacity to cause the harm alleged." Id. In Hanford, for example, the Ninth Circuit explained that the general causation inquiry was "whether exposure to a substance for which a defendant is responsible, such as radiation at the level of exposure alleged by plaintiffs, is capable of causing a particular injury or condition in the general population." Id.

To ultimately prevail in such a lawsuit, however, a plaintiff must show both general and "individual" or "specific" causation. Id. Specific causation refers to whether a particular individual suffers from a particular ailment as a result of exposure to a substance. Id. That is, that the challenged conduct, here, the taking of Celebrex at a certain dose for a particular amount of time, was "the cause-in-fact" of the particular plaintiff's injury. Id.

The parties' motions involve the use of epidemiology to prove causation. "The field of epidemiology addresses the incidence, distribution and etiology (causation) of disease in human populations by comparing individuals exposed to a particular agent to unexposed individuals to determine whether exposure increases the risk of disease." In Re Silicone Gel Breast Implant Prod. Liab. Lit., 318 F.Supp.2d at 892. Scientists use "relative risk" to identify an association between, for example, the ingestion of a drug and

a disease.

> For example, if a study found that 10 out of 1000 women with breast implants were diagnosed with breast cancer and 5 out of 1000 women without implants (the "control" group) were diagnosed with breast cancer, the relative risk of implants is 2.0, or twice as great as the risk of breast cancer without implants. This is so, because the proportion of women in the implant group with breast cancer is 0.1 (10/1000) and the proportion of women in the non-implant group with breast cancer is 0.05 (5/1000). And 0.1 divided by 0.05 is 2.0.

Id. A relative risk of 1.0 suggests that there is no association between the product and the disease, that is, the same numbers of people using the product are diagnosed with the disease as those not using the product. Similarly, a relative risk of less than 1.0 suggests that the product is actually "protective" of the disease: fewer people using the product contract the disease than those not taking the product. Id. at n.5.

In general, epidemiology studies are probative of general causation: a relative risk greater than 1.0 means the product has the capacity to cause the disease. "Where the study properly accounts for potential confounding factors and concludes that exposure to the agent is what increases the probability of contracting the disease, the study has demonstrated *general* causation–that exposure to the agent is capable of causing [the illness at issue] in the general population." Id. at 893 (internal quotation marks and citation omitted).

Such studies can also be probative of specific causation, but only if the relative risk is greater than 2.0, that is, the product more than doubles the risk of getting the disease.

> When the relative risk is 2.0, the alleged cause is responsible for an equal number of cases of the disease as all other background causes present in the control group. Thus, a relative risk of 2.0 implies a 50% probability that the agent at issue was responsible for a particular individual's disease. This means that a relative risk that is greater than 2.0 permits the conclusion that the agent was more likely than not responsible for a particular individual's disease.

Id. at 893. The issue on these motions, however, is not specific causation; there is no particular plaintiff before the Court. Rather, the primary issue is whether the Court should permit plaintiffs' experts to testify that Celebrex is capable of causing

heart attacks or strokes at certain doses.

EPIDEMIOLOGY STUDIES AND TERMS

Before discussing the parties' motions, it is important to identify the different epidemiology studies relied upon by the experts. There are generally three types of clinical epidemiology studies at issue on the parties' motions: (1) randomized controlled clinical trials, (2) observational studies, and (3) meta-analyses.

The "gold standard" for determining whether a drug is related to the risk of developing an adverse health outcome is a "randomized clinical trial" in which the subjects are randomly assigned to one of two groups: one group exposed to the drug of interest and the other not exposed. After a period of time the study participants in both groups are evaluated for an adverse health outcome. Federal Judicial Center, Reference Manual on Scientific Evidence 338 (2d ed. 2000). "Randomization minimizes the likelihood that there are differences in relevant characteristics between those exposed to the agent and those not exposed," such as smoking, obesity, aspirin use and so on that could account for any difference in outcomes between the two groups. Id.

An "observational study" evaluates causation by comparing the risk of disease between patients exposed to a given substance and patients who were not exposed. The study may be prospective, identifying patients and then following them for a period of time, or restrospective, identifying patients and then performing a medical chart review to determine what happened during the period they did or did not take the drug. The downside to observational studies is that because the investigators do not control who participates in the study, it is more difficult to control for confounding factors such as smoking, obesity and the like. The investigator attempts to address the possible role of confounding factors "by considering them in the design of the study and in the analysis and interpretation of the study results." Id. at 339.

There are two types of observational studies: a cohort study and a case control study. A cohort study identifies patients who are taking the drug (exposed) and follows them for a certain amount of time to determine if they have the alleged bad outcome, here,

such outcome is heart attack or stroke. The cohort study also identifies people not taking the drug and follows them (unexposed). The study then compares the rate of the alleged bad outcomes in group one with the rate in group two to compute the "relative risk." Id. at 339-40.

A case control study identifies persons who had a bad outcome (the cases), for example, patients in the United Kingdom database that had a heart attack within the last three years, and reviews their medical records to determine how many of those persons were taking the studied drug around the time of their heart attack. The study then identifies an equal number of people who did not have a heart attack (the controls) and determines how many of them were taking the drug. Id. From those figures an "odds ratio" is computed. For example, if the percentage of people taking Celebrex in both groups is the same, the odds ratio is 1.0; that is, taking Celebrex did not increase the risk of heart attack.

Sometimes randomized controlled studies and observational studies of the same drug will have conflicting results; some will show a statistically significant association while others will not. A meta-analysis pools the results of various studies to arrive at a single figure to represent the totality of the studies reviewed. "In a meta-analysis, studies are given different weights in proportion to the sizes of their study populations and other characteristics." Id. at 380. Meta-analysis has the advantage of pooling more data so that the results are less likely to be misleading solely due to chance. On the other hand, one problem with meta-analysis, particularly in meta-analysis of observational studies, is that the pooled studies often use disparate methodologies.

When reviewing the results of a study, whether it is a randomized clinical trial, observational trial, or a meta-analysis of such trials, it is important to consider the confidence interval. The confidence interval is, in simple terms, the "margin of error." So, for example, if a given study showed a relative risk of 1.40 (a 40 percent increased risk of adverse events), but the 95 percent confidence interval is .8 to 1.9, we would say that we are 95 percent confident that the true value, that is, the actual relative risk, is

between .8 and 1.9. Because the confidence interval includes results which do not show any increased risk, and indeed, show a decreased risk, that is, it includes values less than 1.0, we would say the study does not demonstrate a "statistically significant" increased risk of an adverse outcome. Confidence intervals are calculated, in part, based on the number of people and events included in the study. "The larger the sample size in a study (all other things being equal), the narrower the confidence boundaries will be (indicating greater statistical stability), thereby reflecting the decreased likelihood that the association found in the study would occur if the true association is 1.0 [no increased or decreased risk]." Id. at 361.

With these terms in mind, the Court now turns to the parties' motions.

DISCUSSION

I. Pfizer's Motion

A threshold question raised by Pfizer's motion is whether a particular dose of Celebrex is relevant to the general causation inquiry. Pfizer seeks to exclude any opinion that Celebrex is capable of causing heart attacks and strokes at 200 mg/d as well as any opinion that Celebrex is capable of causing heart attacks and strokes at 400 mg/d. It does not move to exclude expert testimony that Celebrex is capable of causing heart attacks and strokes when a patient ingests 800 mg/d, at least when taken over many months. Thus, Pfizer's motion assumes that Celebrex at different doses can have different cardiovascular effects.

The Court finds that dose matters. All of plaintiffs' experts, with perhaps a single exception, agree that there is a dose effect with Celebrex; that is, that it is more toxic, and is therefore more likely to cause an adverse side effect, when taken at greater doses. See Reference Manual on Scientific Evidence at 403 ("There are three central tenets of toxicology. First, 'the dose makes the poison'; this implies that all chemical agents are intrinsically hazardous--whether they cause harm is only a question of dose. Even water, if consumed in large quantities, can be toxic."); see also Mitchell v. Gencorp, 165 F.3d 778, 781 (10th Cir. 1999) (noting that to prevail in a toxic tort case a "a plaintiff must

demonstrate 'the levels of exposure that are hazardous to human beings generally as well as the plaintiff's actual level of exposure to the defendant's toxic substance before he or she may recover") (internal quotation marks and citation omitted); Allen v. Penn. Eng'g Corp., 102 F.3d 194, 199 (5th Cir. 1996) (explaining that in toxic tort cases, "[s]cientific knowledge of the harmful level of exposure to a chemical plus knowledge that plaintiff was exposed to such quantities are minimal facts necessary to sustain the plaintiff's burden"); see also Hanford Nuclear Reservation Lit., 292 F.3d at 1133 (explaining that the general causation inquiry is whether exposure to the challenged substance "*at the level of exposure alleged by the plaintiffs*" is capable of causing the alleged injuries") (emphasis added). As plaintiffs' cardiology expert, Dr. Neil Doherty, testified: it is a "fundamental principal of medicine" and "medical causality" that the risk of adverse cardiovascular events with Celebrex is dose-related. Transcript of October 10, 2007 Hearing ("Oct. 10 TR") at 328. Thus, the Court must analyze plaintiffs' experts' opinions as to causation at 200 mg/d separate from their opinions as to 400 mg/d.

A. 200 mg/d

Celebrex at 200 mg/d and the risk of adverse cv events has not been studied in published, large, long-term randomized controlled trials. Nonetheless, included in the record are approximately 30 unpublished randomized controlled trials, albeit of short duration and small size. These studies do not demonstrate any association between Celebrex and adverse cv outcomes. A meta-analysis of all available published and unpublished randomized clinical trials of all COX-2 inhibitors as well as traditional NSAIDs found that while COX-2 inhibitors as a whole are associated with a moderate increase in the risk of adverse cv events, no such association is found with the available data for Celebrex at 200 mg/d or less. [1]

The record also includes observational studies with Celebrex data, mostly at 200

[1] Patricia Kearney, et al., Do selective cycol-oxygenase-2 inhibitors and traditional non-steroidal ant-inflammatory drugs increase the risk of atherothrombosis? Meta-analysis of randomized trials, British Medical Journal 2006, June 3; 332(7553): 1302-8.

mg/d. These observational studies together include more than 8,000 adverse cv events, and all of the studies with the most events demonstrate no statistically significant association between Celebrex at 200 mg/d and adverse cv events. A meta-analysis performed by an independent researcher unaffiliated with Pfizer ("McGettigan") concluded that while Vioxx does increase the risk of adverse cv events, "[i]n doses of around 200 mg/d, [Celebrex] was not associated with an increased risk . . . ."[2] Another meta-analysis of eight observational studies showed no increased risk from Celebrex 200 mg/d compared to patients taking no medication.[3]

In sum, there are no randomized controlled trials or meta-analyses of such trials or meta-analyses of observational studies that find an association between Celebrex 200 mg/d and a risk of heart attack or stroke. And most observational studies, indeed, the observational studies that include 97 percent of the reported adverse cv events, also find no statistically significant association. It is thus unsurprising that most of plaintiffs' experts agree that the available evidence at 200 mg/d is inadequate to prove causation. See Deposition Testimony of Dr. Joel Bennett at p. 537, Brown Reply Decl. Exh. 108 ("I think that if you look at all the evidence, I think at 200 milligrams it's hard to make a case that Celebrex has toxicity. It doesn't mean that, again, that in individual cases it couldn't, it could be lost in the big scheme of things, but, in fact, the data don't suggest that in a large population it increases the risk."); Deposition Testimony of Dr. Lemue Moye at p. 268, Brown Reply Decl. Exh. 109 ("[T]here's no study that convincingly demonstrates a signal of cardiovascular events at very low does such as 200 per day."); Deposition Testimony of Dr. Nicholas Jewell at p. 130, Brown Reply Decl. Exh. 110 (when asked whether there is reliable scientific evidence to establish that 200 mg/d causes heart attacks and strokes he responded that the evidence is not sufficient "to be definitive"); Deposition

[2] Patricia McGettigan, et al., Cardiovascular Risk and Inhibition of Cyclooxygenase: A Systematic Review of the Observational Studies of Selective and Nonselective inhibitors of Cyclooxygenase 2, JAMA 2006 Oct 4; 296(13): 633-44.
[3] S. Hernandez-Diaz et al., Non-steroidal anti-inflammatory drugs and the risk of acute myocardial infarction, Basic Clin. Pharmacol. Toxicol. 2006 Mar; 98(3):266-274, at 270, 273.

of Dr. James M. Wright at pp. 83-84, 92, Brown Decl. Reply Exh. 106 (stating that it has not been proven that at 200 mg/d Celebrex increases the risk of heart attack because "we don't have enough information").

1. Dr. Neil Doherty

Plaintiffs' cardiology expert, Dr. Neil Doherty, nonetheless asserts "to a reasonable degree of medical probability that the 200 mg dose of Celebrex can increase the risk of MI's [heart attacks]." Written Direct Examination of Dr. Neil F. Doherty III ("Doherty Written Direct") at ¶ 18. He reaches his opinion by first identifying his conclusion—causation at 200 mg/d—and then cherry-picking observational studies that support his conclusion and rejecting or ignoring the great weight of the evidence that contradicts his conclusion. Dr. Doherty's opinion does not reflect scientific knowledge, is not derived by the scientific method, and is not "good science;" it is therefore inadmissible.

First, Dr. Doherty is not qualified to favor certain observational studies over the great weight of the epidemiologic evidence to give an opinion on causation. He is a clinical cardiologist who sees patients 95 percent of his physician time. He does not have any specialized epidemiology training. He has not published any research since 1992, and his 13 publications are unrelated to the subject matter of these lawsuits. He has never participated in an observational study of any kind. He is therefore not qualified to opine that one or two observational studies are correct while all the other studies (the studies that include 97 percent of the adverse cv events) are wrong. Moreover, he only became interested in Celebrex and cv risk *after* he was retained by plaintiffs in this litigation; indeed, although the issue of COX-2 inhibitors and adverse cv events has been well known since at least 2005, he did not discontinue prescribing Celebrex until after plaintiffs retained him as an expert in this case. Doherty Written Direct at ¶ 2. Dr. Doherty's opinion was developed for the purpose of this litigation. See Daubert II, 43 F.3d at 1317 ("One very significant fact to be considered is whether the experts are proposing to testify about matters growing naturally and directly out of research they have conducted independent of the litigation, or whether they have developed their opinions

expressly for purposes of testifying.").

Second, apart from his lack of relevant experience and training (or because of it), the foundation of his opinion--wholly rejecting the McGettigan meta-analysis and the other observational studies that do not support his opinion--is not a scientifically valid methodology. For example, while he justifies his wholesale rejection of McGettigan on the blanket ground that meta-analysis is inappropriate for observational studies, plaintiffs' other experts rely on such studies; indeed, Dr. Bennett testified that McGettigan is a "good study." Dr. Bennett Depo. at p. 187-88, Brown Reply Decl. Exh. 108. And the American Heart Association Committee that developed a "Science Advisory" on the use of NSAIDs also relied on McGettigan. Finally, Dr. Doherty testified that he prefers the Oxford Centre for Evidence Based Medicine ranking of the levels of evidence that a scientist should consider. Doherty Written Direct at ¶ 21-22. That ranking identifies systematic review, including meta-analysis, as the highest level for each category of evidence. Oct. 10 TR at 350.

Third, Dr. Doherty testified that the "strongest evidence" for his 200 mg/d opinion "is the Andersohn study published in Circulation in 2006."[4] Doherty Written Direct at ¶ 18. He attempts to justify his heavy reliance on Andersohn by asserting that it is the "best designed" of all the observational studies. When asked why, however, Dr. Doherty responded only that the study is derived from the United Kingdom database which is among the most complete in the world. Oct. 10 TR at 309-10. He also mentioned that Andersohn is a prospective, rather than retrospective study. Id. at 310. But many of the other studies he rejects out of hand are also prospective, and he does not cite anything in the medical literature that suggests that it is a valid scientific method to prefer one study over many that have contradictory results simply because the study that supports the expert's conclusion utilized the United Kingdom database.

[4] Frank Andersohn, et al., Use of First-and Second-Generation Cyclooxygenase-2-Selective Nonsteroidal Anti-inflammatory Drugs and Risk of Acute Amuyocardial Infarction, Circulation, 2006 Apr 25; 113(16): 1950-7.

Fourth, Dr. Doherty's reliance on Andersohn as "the strongest evidence" of an increased risk at 200 mg/d is undermined by his own testimony that Andersohn's results do not make "biological sense." Oct. 10 TR at 363-64. Andersohn found the increased risk of heart attack was higher at shorter durations of use (less than three months) than at higher durations; indeed, there was no statistically significant association at durations greater than three months, a finding that directly contradicts Dr. Doherty's testimony that the risk of heart attack increases with duration of use. Oct. 10 TR at 359-61. Andersohn also found that the risk of heart attack is statistically significant in patients without cv risk factors, but is not statistically significant in patients with such risk factors. Id. at 364. Again, this finding directly contradicts Dr. Doherty's testimony that the risk of heart attack from Celebrex is greater in patients with heart disease. To conclude that Celebrex 200 mg/d causes heart attacks and strokes based on a study that does not make "biological sense" is not sound science.

Fifth, Dr. Doherty's opinion is based on his fundamental misunderstanding of Andersohn. Dr. Doherty testified that Andersohn is a cohort study and he "puts a lot more weight" into cohort studies as opposed to case control studies. Oct. 10 TR at 255, 309, 350. He repeatedly testified that he relies on Andersohn out of all of the available evidence because it is a good cohort study. See, e.g., id. at 313, 315. When he was confronted with Andersohn's own description of the study, however, Dr. Doherty conceded that Andersohn is not a cohort study, but is instead "a case-control study nested within a cohort study." Id. at 352.

Dr. Doherty also insisted that Andersohn used cox proportional hazard analysis, the analysis most commonly used for cohort studies. Oct. 10 TR at 320-21, 355. On cross-examination, however, he could not identify where in the study the authors disclose that they used cox-proportional hazard analysis and Dr. Doherty pointedly did not clarify his testimony on re-direct. The Court has reviewed Andersohn and it does not indicate that the study authors used cox-proportional hazard analysis; rather, they used logistic regression which resulted in an "odds ratio," an analysis consistent with case control

studies. Dr. Doherty's fundamental misunderstanding of the study he "relied most strongly on" to support his opinion, Doherty Written Direct at ¶ 31, is perhaps explained by his inability to explain the difference between a cohort study and case control study "off the top of his head," Oct. 10 TR at 348, and his inability to define the cox proportional hazards model or explain logistic regression analysis. Id. In any event, as Andersohn is a case control study, Dr. Doherty's heavy reliance upon it is unreliable in light of his own blanket rejection of all of the case control studies showing no association between Celebrex 200 mg/d and cv risk on the ground that case control studies are not as reliable as cohort studies. Doherty Written Direct at ¶ 37.

While Andersohn is the "strongest evidence" supporting Dr. Doherty's opinion, he also cited an additional observational study, Gislason.[5] Gislason, however, had few events and merely evaluated COX-2 inhibitors and the risk of a heart attack in patients who had already had a heart attack. Moreover, the study failed to control for smoking, a well-known risk for heart attack, as well as aspirin use, even though another of plaintiffs' experts, Dr. Maryilyn Rymer, criticized another observational study for not adjusting for aspirin use. Dr. Maryilyn Rymer Written Direct Testimony ("Rymer Written Direct") at ¶ 34. In light of these limitations, and the totality of the available evidence, Gislason does not salvage Dr. Doherty's opinion that Celebrex at 200 mg/d can cause heart attacks.

Dr. Doherty also relied on the "imbalance hypothesis" as evidence that it is biologically plausible that Celebrex causes heart attacks. This hypothesis asserts that COX-2 inhibitors as a class, that is, Vioxx, Bextra and Celebrex, create an imbalance in the arteries by blocking prostacyclin (an anti-clotting agent). Under this theory, the imbalance caused by ingesting a COX-2 will lead to an adverse cv event if the patient already has a risk factor, such as high blood pressure, smoking, or high cholesterol. Dr. Doherty argues that this hypothesis means that it makes sense that Celebrex increases the

[5] Gunnar H. Gislason, et al., Risk of Death or Reincarnation Associated With the Use of Selective Cyclooxygenase-2 Inhibitors and Nonselective Nonsteroidal Antiinflammatory Drugs After Acute Myocardial Infarction, Circulation, 2006 June 27; 113(25): 2906-13.

risk of heart attacks and strokes. He did not explain, however, how he reconciles this theory with Andersohn—the strongest evidence of his causation opinion—which showed a greater risk of heart attacks in patients with no cv risk factors.

In any event, both Dr. Doherty and Dr. Joel Bennett—plaintiffs' imbalance hypothesis expert—agree that the only way to prove the hypothesis is to look at the data from epidemiological studies. Oct. 10 TR at 373. For example, Dr. Bennett agreed that the only method available to determine how much Celebrex is needed (that is, what dose) to create an imbalance sufficient to cause a heart attack is patient studies. Oct. 9 TR at 209, 210. As is explained above, the patient studies do not demonstrate an association between Celebrex 200 mg/d and heart attack or stroke; therefore, the imbalance hypothesis—even if true—(and it is only one of many possible explanations for the apparent increased risk of heart attacks from COX-2 inhibitors at certain doses) does not support Dr. Doherty's opinion that Celebrex is capable of causing heart attacks at 200 mg/d.

2. Dr. Maryilyn Rymer

Dr. Maryilyn Rymer's testimony does not provide the missing link. Dr. Rymer is a neurologist and plaintiffs offered her as a stroke expert, essentially to opine that Celebrex causes strokes as well as heart attacks. In her written direct testimony she opines that "the totality of the scientifically reliable evidence supports that [Celebrex] can cause strokes and other cardiovascular events at all therapeutic doses, especially in those individuals who are high risk for cardiovascular events." Rymer Written Direct at ¶ 7. She admits that there is no data from randomized controlled trials to support her conclusion at 200 mg/d; instead, she primarily relies on (1) the imbalance hypothesis, (2) the same Andersohn study upon which Dr. Doherty relies, and (3) the Wellpoint data, an unpublished observational study of unknown design. In other words, Dr. Rymer, as does Dr. Doherty, ignores the vast majority of the evidence in favor of the few studies that support her conclusion.

The Court has already addressed the imbalance hypothesis and the Andersohn

study, neither of which provide scientifically valid support for her opinion in light of the great weight of the epidemiologic evidence. It is worth adding, however, that Dr. Rymer's reliance on the Andersohn heart attack study is inconsistent with her criticism of the Andersohn stroke study. The latter study, performed by the same Andersohn as the heart attack study, indeed, it is the same study but focused on stroke rather than heart attack outcomes, found no statistically significant increased risk of stroke associated with Celebrex use at 200 mg/d. Dr. Rymer criticized the stroke study for not controlling for aspirin use and having a 10 percent error rate; yet the Andersohn heart attack study suffers from the same limitations.

Dr. Rymer relies heavily on an unpublished, non-peer reviewed study from a managed care organization ("the Wellpoint Report"). Dr. Rymer attaches to her written direct testimony a letter from Wellpoint to the FDA summarizing the results of the study. The letter discloses a relative risk from Celebrex use of 1.19 when the data is analyzed to control for "age and other cardiovascular risk factors;" however, this very low risk includes *all* doses of Celebrex. Moreover, the letter does not identify study design, the analysis used, or even the confidence intervals. Dr. Rymer admitted on cross-examination that the study also fails to account for critical compounding factors such as smoking. This unpublished, unreviewed study, which combines all doses of Celebrex, and fails to adjust for critical compounding factors such as smoking, is not a scientifically valid basis for Dr. Rymer's rejection of all the other observational data--including meta-analyses--that do not show a statistically significant increase in the risk of heart attack or stroke at 200 mg/d.

Finally, Dr. Rymer cited Gislason, discussed above, and Brophy,[6] as support for causation at 200 mg/d. Brophy, as Gislason, evaluated the risk of heart attack in patients who had already had at least one heart attack. Brophy, however, did not find a statistically significant increased risk of heart attack at 200 mg/d, even in these high risk

[6] James M. Brophy, The coronary risk of cyclo-oxygenase-2 inhibitors in patients with a previous myocardial infarction. Plaintiffs cited this study as being available at heart.bmj.com or at www.heartjnl.com.

patients. And while it did show a greater risk in the high risk population (although not a statistically significant risk), the higher risk found in Brophy and Gislason is contradicted by the results of at least nine other studies, including Dr. Doherty's "strongest evidence" of causation, the Andersohn heart study. Such data cannot reliably form the basis for rejecting the overwhelming pattern of evidence that fails to show any statistically significant risk at 200 mg/d.

3. Extrapolation

Dr. Doherty, and to some extent Dr. Rymer, also rely on studies of Celebrex 400 mg/d to support their opinion of causation at 200 mg/d. Although Dr. Doherty acknowledges that dose matters with Celebrex, he simply takes the relative risk point estimate of APC for 400 mg/d and cuts it in half (ignoring the confidence interval) to support his opinion that Celebrex at 200 mg/d can cause a heart attack. Oct. 10 TR at 304. When the Court asked Dr. Doherty if there is anything in the scientific literature to support such primitive extrapolation, he failed to identify any scientific support for his method other than his own judgment. Id. at 342-43, 378-79. He also admitted that there is no way of knowing what the confidence interval is for 200 mg/d under his unique methodology. Id. at 340-41. Such an unscientific, untested methodology cannot support the proffered opinion of causation at 200 mg/d, especially where, as here, Dr. Doherty agrees with all the other experts that there is dose effect with Celebrex.

Plaintiffs' reliance on In re PPA Products Liab. Litig., 289 F.Supp.2d 1230 (W.D. Wa. 2003), to argue that causation at 200 mg/d can be inferred from the 400 mg/d data is misplaced. In the PPA multi-district litigation the issue was whether PPA, a drug used in cough and cold and appetite suppressant products, can cause strokes. Plaintiffs' experts' opinion that PPA can cause strokes in persons of all ages and genders was based primarily upon a study of women ages 18 to 49. Id. at 1235-36. While men were not excluded from the study, their participation was too low to draw any conclusions. Id. at 1236. The defendants argued that the evidence was therefore insufficient to support the plaintiffs' experts' opinions that PPA can cause strokes in persons of all ages and genders. Id. at

1244. The district court disagreed.

The court found that "it is scientifically acceptable to extrapolate the conclusions of the [study] to these sub-populations." Id. at 1244. As to persons older than 49, the court noted that there are no known studies that suggest that drugs get safer as persons get older; thus, it made common scientific sense to extrapolate the results of the study to persons over 49. Id. Plaintiffs' experts also attested to the "commonplace" practice of extrapolating between the genders based on "the historical exclusion of women from scientific studies." Id.

The justification for extrapolating drug effects between biologically similar demographic groups, however, does not logically extend to the argument that all doses of a compound are harmful; accordingly, plaintiffs' experts could not cite to a single piece of evidence that suggests that their experts' extrapolation is scientifically valid. To the contrary, with nearly all compounds there is usually a threshold that must be met before there is any harm; for example, even water can be harmful if consumed at certain amounts even though there is no harm at smaller amounts. Dr. Doherty claimed that the threshold for Celebrex must be 50 mg/d because that is the dose that is effective for pain relief. That "theory," however, is nothing more than Dr. Doherty's wholly untested, unpublished, and non-peer reviewed justification for his reliance on the 400 mg/d data. Moreover, the great weight of the evidence does not support the extrapolation, that is, studies show that there is no statistically significant association between Celebrex 200 mg/d and the risk of strokes or heart attacks.

Instead of citing evidence that supports such extrapolation, plaintiffs complain that the evidence of harm at 200 mg/d does not exist because Pfizer did not initiate long term randomized trials at such dose. Such a trial, known as PRECISION, is now underway, but the results will not be available for some time. Plaintiffs cite no case, however, that suggests that they can satisfy their burden of proof based on a lack of evidence; plaintiffs filed these lawsuits and plaintiffs carry the burden of proving today based on currently available scientifically valid evidence that Celebrex can cause heart attacks or strokes at

200 mg/d.

Plaintiffs have not met their burden. In so finding, the Court is relying on the evidence presented by plaintiffs; it has not considered Pfizer's own meta-analyses. And the Court's ruling is not mandated by the lack of randomized clinical trials that show an association at 200 mg/d; plaintiffs could still meet their burden in the absence of such evidence. See Kennedy v. Collagen Corp., 161 F.3d 1226, 1228 (9th Cir. 1998). However, the opinion of Dr. Doherty and Dr. Rymer that Celebrex 200 mg/d increases the risk of heart attacks or strokes is not based on a scientific valid methodology; instead, these experts ignore the great weight of the observational studies that contradict their conclusion and instead rely on the handful that appear to support their litigation-created opinion. As the Court explained above, their reasons for doing so are not supported by scientifically valid reasons or methodology. In the words of the Supreme Court, the "analytical gap" between the data and these experts' conclusion is simply too great to make the opinion admissible. General Elect. Co. v. Joiner, 522 U.S. 136, 146 (1997).

B. 400 mg/d

Pfizer's motion to exclude expert testimony that Celebrex 400 mg/d is capable of causing heart attacks or strokes is defeated by APC, a large, long-term, randomized, placebo-controlled, double-blind, multi-center clinical trial that was halted after 33 months because it demonstrated a statistically significant risk of heart attack, stroke, and heart failure at 400 mg/d (2.6 percent hazards ratio with a confidence interval of 1.1 to 6.1) and 800 mg/d (3.4 percent hazards ratio with a confidence interval of 1.5 to 7.9).[7] The study, co-sponsored by the National Cancer Institute and Pfizer, was designed to compare Celebrex with placebo for the prevention of colorectal adenomas (polyps). The study included a "cardiovascular safety committee" that developed guidelines to evaluate cardiovascular safety. On December 16, 2004, on the basis of the results then available as

[7] Scott D. Solomon, et al., Cardiovascular Risk Associated with Celecoxib in a Clinical Trial for Colorectal Adenoma Prevention, N. Engl. J. Med. 2005 Mar 17; 352(11): 1071-1080.

well as studies of Vioxx and Bextra, and on the recommendation of the safety committee, the APC steering committee stopped the trial. This randomized, placebo-controlled, double-blinded study with an independent committee evaluating cardiovascular endpoints is the "gold standard" of epidemiologic evidence and supports plaintiffs' experts' testimony that Celebrex at 400 mg/d is capable of causing heart attacks or strokes.

Pfizer nonetheless contends that plaintiffs' experts' opinion must be excluded because (1) APC was stopped early, and (2) its results have not been replicated by two other randomized controlled trials that evaluated Celebrex 400 mg/d: ADAPT and PreSAP.

The Court is unconvinced that plaintiffs' experts cannot base their opinions on APC because it was stopped early (after 33 months). The APC steering committee halted the trial because the evidence of harm was so significant. To exclude reliance on such studies under these circumstances would mean the more harmful the drug the more difficult it is to prove harm. While such studies must be closely scrutinized due to their early termination, Pfizer's argument goes to the study's weight; Pfizer has not shown that it is not scientifically valid for plaintiffs' experts to rely on the results. Moreover, ADAPT and PreSAP, two studies upon which Pfizer relies, were also halted early because of the APC results.

The Court is also not persuaded that the failure of ADAPT and PreSAP to replicate APC's results means plaintiffs' expert opinion on 400 mg/d is inadmissible. ADAPT was a randomized, placebo-controlled clinical trial designed to evaluate naproxen and Celebrex 400 mg/d (200 mg twice daily) and the prevention of Alzheimer's dementia.[8] ADAPT found a hazards ratio for Celebrex of 1.10 percent with a confidence interval of .67 to 1.79, that is, no statistically significant association. The study authors, however, cautioned that there are several limitations to their data. First, ADAPT was not designed

[8] ADAPT Research Group, Cardiovascular and Cerebrovascular Events in the Randomized, Controlled Alzheimer's Disease Anti-Inflammatory Prevention Trial (ADAPT), PLoS Clin Trials 2006; 1(7): e33.

to detect differences in cardiovascular and cerebrovascular risks and, unlike APC, it did not include a separate cardiovascular safety committee tasked solely with evaluating cardiovascular outcomes. Second, and, according to the authors, the largest limitation of the data is the small number of cardiovascular events. Third, an editorial comment accompanying the study suggests that because study participants eligible to join the trial were required to have a family history of Alzheimer's disease, it is possible the study participants' risk factors differed from the general population. The results of ADAPT need to weighed with the APC results, but ADAPT's conclusions do not make reliance on APC scientifically invalid.

The results of PreSAP, a randomized controlled study with fewer participants than ADAPT or APC, also did not replicate the APC results. PreSAP, as APC, was designed to evaluate Celebrex's effect on the occurrence of colorectal adenomas. Preliminary results from that study did not show a statistically significant increase in cv risk for patients taking Celebrex 400 mg/d, but did not exclude the possibility of a hazards ratio similar to that demonstrated by APC. In addition, PreSAP used the same independent cardiovascular safety committee as APC to assess the risk of Celebrex on adverse cv events. Accordingly, the data from both trials were synthesized to produce a combined estimate of risk of cardiovascular death, heart attack, stroke or heart failure of 1.9 with a confidence interval of 1.1 to 3.1; in other words, combining the raw data showed a statistically significant increase in risk.[9] The study authors combined APC 400 mg/d and 800 mg/d with PreSAP 400 mg/d because the confidence intervals for 400 mg/d and 800 mg/d substantially overlapped. While the weight to be given to this evidence can be argued, in light of this evidence, and the Kearney meta-analysis which found a relative risk greater than one with a confidence interval that barely crossed one, the Court cannot conclude that expert opinion that Celebrex 400 mg/d is capable of causing heart attacks

[9] Scott D. Solomon, et al., Effect of Celecoxib on Cardiovascular Events and Blood Pressure in Two Trials for the Prevention of Colorectal Adenomas, Circulation, 2006 Sep 5; 114(10): 1028-35.

and strokes is scientifically invalid.

C. Whether Celebrex Causes Heart Attacks or Strokes More Than Three Days After A Patient Stops Taking It

Plaintiffs do not dispute that Celebrex is not capable of causing hearts attacks or strokes more than three days after a patient stops taking it and they have offered no expert opinion to the contrary. Accordingly, there is no proposed expert testimony on this issue for the Court to exclude.

D. Remaining Issues

1. Strokes

The issue as to whether Celebrex is capable of causing strokes is close. Plaintiffs rely on the testimony of Dr. Rymer, a neurologist and the Medical Director of the Saint Luke's Brain and Stroke Institute at Saint Luke's Hospital in Kansas City, Missouri. She testified that the mechanism of and risk factors for throembolic strokes (excluding cardiogenic embolism) and heart attacks are the same; thus, if Celebrex causes an increased risk in heart attacks it also increases the risk of strokes. Rymer Written Direct ¶ 11-13. Dr. Rymer's testimony is supported by the published literature as nearly all studies of COX-2 inhibitors and cv risk lump strokes together with heart attacks. For example, the Kearney meta-analysis of clinical trials identified the relative risk for "serious vascular events," defined as heart attack, stroke, or vascular death. Indeed, even Pfizer's expert, Dr. Packer, considers the risk of heart attacks and strokes together, and Pfizer does not dispute Dr. Rymer's testimony as to the similar mechanism of heart attacks and strokes.

Pfizer nonetheless asserts that Dr. Rymer's testimony is inadmissible because the randomized controlled trials and observational studies that do separately report strokes and heart attacks do not suggest an association between Celebrex at any dose and strokes. Dr. Rymer explains, however, that none of the randomized controlled studies was designed to look for stroke outcomes, and strokes occur far less often than heart attacks; the studies simply were not designed to find an association or not.

While there is some epidemiologic evidence to dispute her mechanism testimony, that is, evidence that suggests that even though heart attacks and certain strokes are caused by the same mechanism Celebrex does not cause both, there is also some evidence to support her testimony. On the current record the Court does not find that Dr. Rymer's testimony is scientifically invalid and inadmissible. See Daubert, 509 U.S. at 596 ("Vigorous cross-examination, presentation of contrary evidence, and careful instruction on the burden of proof are the traditional and appropriate means of attacking shaky but admissible evidence.").

2. Duration

The Court also denies Pfizer's motion to exclude testimony that Celebrex is capable of causing heart attacks or strokes only after 33 months of continuous use. Because a statistically significant association did not appear in APC until after 33 months does not mean as a matter of scientific fact that none of the adverse cv events that occurred after a shorter duration were not caused by the patient's ingestion of Celebrex.

3. Specific Causation

Finally, Pfizer asks the Court to "exclude any opinion that Celebrex caused an individual plaintiff's heart attack or stroke absent a relative risk that exceeds 2.0." This is a question of specific causation as to particular plaintiffs; as the Court does not have before it evidence as to any specific plaintiff the Court declines to grant Pfizer's motion.

II. Plaintiffs' Motion to Exclude

Plaintiffs move to exclude the meta-analyses performed by Pfizer's experts. Plaintiffs' experts did not perform any of their own meta-analyses; instead, plaintiffs attack Pfizer's experts' methodologies. Plaintiffs' motion is denied. All of plaintiffs' arguments go to the weight a trier of fact gives to the meta-analyses. Plaintiffs have not shown that the methods employed by Pfizer's experts are not based on good science.

Plaintiffs also move to exclude Dr. Packer from testifying as to an alternative theory to the imbalance hypothesis. Dr. Packer's explanation, which accounts for the difference in outcomes between Vioxx and Celebrex, is based on increased blood

pressure, a theory actually supported by plaintiffs' expert Dr. Rymer. In any event, Dr. Packer's testimony satisfies Daubert.

CONCLUSION

In Daubert, the Supreme Court held that federal judges perform a gatekeeping role, 509 U.S. at 597, and "to do so they must satisfy themselves that scientific evidence meets a certain standard of reliability before it is admitted." Daubert II, 43 F.3d at 1316. Plaintiffs' expert testimony that Celebrex 200 mg/d can cause heart attacks or strokes does not meet that standard. Dr. Doherty, a clinical physician with no relevant research experience and who developed his opinion for the purpose of testifying, bases his opinion on a study that he fundamentally misunderstood, is counter to the great weight of the evidence, and, by his own admission, does not make biological sense. The Court cannot find that his opinion is good science. Dr. Rymer's 200 mg/d opinion is also not good science. She ignores all the evidence that contradicts her litigation-created conclusion and instead bases her opinion on the same cherry-picked study as Dr. Doherty, even though that study suffers from the exact same limitations that caused her to reject other studies that do not support her conclusion. She also relies on an unpublished, non-peer reviewed study that does not disclose its design or confidence intervals. If the Court's gatekeeping function means anything, it must mean that these unreliable opinions are not admissible to prove general causation at 200 mg/d.

In all other respects, and for the reasons explained above, the parties' motions are denied.

IT IS SO ORDERED.

Dated: November 19, 2007

/s/
HONORABLE CHARLES R. BREYER
UNITED STATES DISTRICT JUDGE

EXHIBIT E

JAMA & ARCHIVES JOURNALS
American Medical Association

Jose, P. Thornton, JD
Editorial Counsel

312 464-4609 Fax 312 464-4073
joseph.thornton@jama-archives.org

SCIENTIFIC PUBLICATIONS & MULTIMEDIA APPLICATIONS
515 North State Street Chicago, IL 60610 USA

September 7, 2007

Ms. Jennifer Squillario
DLA Piper US LLP
The Marbury Building
6225 Smith Avenue
Baltimore, MD 21209-3600

RE: Objections to JAMA Subpoenas
In re: Bextra and Celebrex Marketing Sales Practices and Product Liability Litigation, MDL 1699

Dear Ms. Squillario:

I write to confirm our conversation of August 23, 2007 and to set forth the multiple objections we assert regarding two subpoenas issued in the above MDL matter. I had earlier discussions with your colleague, Heather Olson, a DLA attorney in your Philadelphia office, about our objections, and Ms. Olson reached a stand down agreement while those objections were being considered.

As mentioned, I am Editorial Counsel for the Journal of the American Medical Association [JAMA] and the Archives of Internal Medicine. While published by the AMA, these journals are part of a separate division of the AMA directed by the Editor-in-Chief of JAMA, Dr. Catherine DeAngelis. Dr. DeAngelis also serves as an AMA Senior Vice President. I am advising the Editor-in-Chief and appearing as counsel for both journals in regard to these subpoenas. For convenience, I shall refer to them as the JAMA subpoenas.

I understand you are the point person among counsel for the defendants regarding discovery in the above captioned matter, and now have the responsibility Ms. Olson did when I spoke with her in June, 2007. Previously, Ms. Olson represented that she had authority to negotiate with me about the subpoenas, rather than Matthew Sullivan, the attorney at Winston & Strawn who issued and served the JAMA subpoenas.

Since you are replacing Ms. Olson as my contact, please confirm that you likewise have the authority on behalf of defense counsel to modify or withdraw the subpoenas, and to waive or negotiate the scope of acceptable compliance. I understand that you may wish

to consult colleagues before reaching and communicating any decisions, perhaps the DLA partner who is Defendants' Liaison Counsel, but I need to be able to rely upon any understanding you and I might reach.

For the record, on June 7, 2007, Ms. Olson informed me that:

1. DLA was primarily interested in "documents" rather than witnesses. Indeed, she indicated that despite the reference to FRCP 30(b)(6), she waived the obligation to produce witnesses on the return date.

2. That the June 11, 2007 return date in the subpoenas for the production of documents was suspended, as confirmed by the enclosed June 8 email. I presented our claims of privilege and objections orally on June 7, but as Ms. Olson was recovering from an unexpected hospital stay, we did not have any further discussions of substance. We did not agreed on an adjourned date and the suspension of production of documents has remained in effect.

When you called me on August 23, 2007, you acknowledged you were aware of our objections and claims of privilege, even mentioning you aware of the Illinois Reporter's Privilege Act, 735, Ill. Comp. Stat. Ann. 5/8-901 et seq., and the opinion that confirmed it was available to JAMA, Cukier v. American Medical Association, the Journal of the American Medical Association, et al., 259 Ill. App.3d 159 (Ill. App. 1994).

You expressed an interest in obtaining documents for which we did not assert a privilege, and we are willing to produce them, toward a resolution of this matter. It does neither of our clients any good to leave the subpoenas hanging indefinitely, and we request that you withdraw the subpoenas, or announce you are satisfied with our partial production, as you receive them. We propose partial production without waiving our rights to object to the JAMA subpoenas.

For the record, we object to the two subpoenas and rely upon several privileges which we believe prevent disclosure of some of the information and many of the documents otherwise sought by the above subpoenas. In a nutshell, our arguments against compelled disclosure include:

1. The Illinois Reporter's Privilege Act, 735, Ill. Comp. Stat. Ann. 5/8-901 et seq.
2. The Illinois Medical Studies Act, 735 Ill. Comp. Stat. Ann. 5/8-2101 et seq.
3. Case law, such as Cukier v. American Medical Association, the Journal of the American Medical Association, et al., 259 Ill. App.3d 159 (Ill. App. 1994).
4. The peer review process privilege.
5. Ethical rules of confidentiality regarding the editorial evaluation process.
6. Ethical and legal obligations to and among editors and peer reviewers.

Our general objections to the subpoenas include:

7. They call for material that is subject to a variety of common law and statutory privileges; as set forth above;
8. They are overly broad and burdensome, particularly considering the claims and defenses in the pending litigation, and the ten year scope of the subpoenas;
9. They call for information and records that the requesting party knows are available from alternative sources, including the defendants themselves, and experts in their employ;
10. They call for electronically stored information [ESI] that is not reasonably accessible by JAMA because of undue burden or cost; and the ten year scope of the subpoenas;
11. They are not reasonable, as required by FRCP 26, in that they are not specifically tailored to discover from a non party information relevant to a claim or affirmative defense, given defendants possession of the same or similar information and documents, and knowledge of alternative sources that have not been exhausted.
12. Their Instructions purport to require the creation of logs and documents that do not exist and a duty to conduct an unreasonable and unduly burdensome investigation, i.e. Instructions 2, 3, 4, 5 and 6.

I suspect you and your colleagues already possess copies of the few relevant articles actually published in JAMA and the Archives of Internal Medicine, but we can provide additional copies as they are requested by your subpoenas are not privileged.

The subpoena issued to JAMA identifies two manuscripts by name, but describes them as "rejected." I discussed with you and earlier with Ms. Olson, that we cannot confirm or reveal whether a manuscript was submitted for publication, let alone whether it was rejected and, if so, why. To do so would violate the fundamental yet fragile underpinnings of the peer review process. Neither can we disclose documents that would reveal which expert peer reviewers evaluated specific manuscripts.

When I asked Ms. Olson why the lawyers who drafted the JAMA subpoena thought these manuscripts were rejected by JAMA, she reported that the authors said so. If that is accurate, then the defendants must have some sponsorship relationships with these authors, and we cannot comment further, even if the authors are free or duty bound to do so.

We are prepared to produce copies of documents in our possession that respond to the two subpoenas, but are not privileged or the subject of an objection. A package of such documents could be shipped to you in Baltimore or to your local counsel in Chicago. The checks totaling $80.89 that accompanied the subpoenas will not cover the cost of copying plus an overnight carrier, so I would prefer to mail them unless you provide me with a

shipper number. Unless I hear otherwise by September 15th, I shall mail the unprivileged documents to you in Baltimore.

After you receive the documents, I plan to cash the Winston & Strawn checks, while awaiting your review. I sincerely hope you will promptly confirm in writing that our partial compliance is satisfactory, or withdraw the subpoenas. If for some reason you and your colleagues desire to pursue the matter further, I trust you would not do so before seriously considering our asserted objections and privileges.

We believe your obligation to make third party discovery demands reasonable includes the exhaustion of all alternative sources. Now that we have asserted the reporters privilege, under the Illinois statute you must file an application demonstrating your compliance with the statute as a condition to pursuing access.

Should you wish to discuss this matter further, I would welcome your call.

Sincerely,

Joseph P. Thornton

Joseph P. Thornton
Editorial Counsel

Enclosure

Joseph Thornton

From: Joseph Thornton
Sent: Friday, June 08, 2007 11:13 AM
To: Olson, Heather R .
Cc: msullivan@winston.com
Subject: suspension of return date on Celebrex subpoenas

Dear Ms. Olson and Mr. Sullivan:

I write to confirm my conversation yesterday with Heather Olson regarding the subpoenas issued to JAMA and the Archives of Internal Medicine in the MDL 1699 Bextra and Celebrex case.

Ms. Olson and I agreed that the June 11th return date on those subpoenas has been extended or suspended while she considers objections I raised and privileges I asserted when we spoke. There are a number of published and non-privileged materials I can produce, but we agreed to defer partial compliance while Ms. Olson consults her colleagues.

Matthew, I am copying you on this email with Heather's knowledge so you understand there will be no appearances on Monday, June 11th, and can cancel the court reporter, if you have not already done so. Heather confirmed that her primary interest was in documents, not witnesses, anyway, and I plan to propose the use of cover letter from me as the vehicle for producing the responsive documents at the appropriate time.

Heather agreed to determine whether other attorneys, including plaintiffs' counsel, needed to be alerted to this agreement that the production deposition we not occur on Monday. I plan to send Ms. Olson a letter recapping the objections and asserted privileges, so she may consider our position and authorities, and then we can further discuss next steps. Thank you.

Joseph P. Thornton, JD
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EXHIBIT F

JAMA & ARCHIVES JOURNALS
American Medical Association

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SCIENTIFIC PUBLICATIONS & MULTIMEDIA APPLICATIONS
515 North State Street Chicago, IL 60610 USA

September 14, 2007

Ms. Jennifer Squillario
DLA Piper US LLP
The Marbury Building
6225 Smith Avenue
Baltimore, MD 21209-3600

RE: Production of Non-Privileged Documents
In re: Bextra and Celebrex Marketing Sales Practices and Product Liability Litigation, MDL 1699

Dear Ms. Squillario:

As promised in my letter of September 7, 2007, I am enclosing copies of non-privileged documents that response to the subpoenas issued to JAMA and the Archives of Internal Medicine. We continue to rely upon the objections and privileges asserted in the September 7 correspondence, and this partial production is not and cannot be viewed as a waiver of any of the asserted objections and privileges.

We shall negotiate the two, small checks forwarded toward covering the costs of photocopying. We submit the enclosed documents in satisfaction of your subpoenas and shall consider the matter closed until and unless we hear from you regarding a possible motion, application or fresh subpoena. Thank you.

Sincerely,

Joseph P. Thornton

Joseph P. Thornton
Editorial Counsel

Enclosures

SEP 19 2007

EXHIBIT G

DLA PIPER

DLA Piper US LLP
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Jennifer K. Squillario
jennifer.squillario@dlapiper.com
T 410.580.4145
F 410.580.3145

September 21, 2007

VIA First Class Mail

Joseph P. Thornton
Editorial Counsel
JAMA & Archives Journals
515 North State Street
Chicago, IL 60610

Re: JAMA and Archives of Internal Medicine Subpoenas, In re: Bextra and Celebrex Marketing Sales Practices and Product Liability Litigation, MDL No. 1699

Dear Mr. Thornton:

Thank you for the recent production of documents in partial satisfaction of the subpoenas served upon the Journal of the American Medical Association (the "JAMA") and the Archives of Internal Medicine (the "AIM") (collectively the "Journals") on behalf of Pfizer Inc. ("Pfizer"). Since our last contact, we have had the opportunity to consider the privileges you asserted in objection to the subpoenas, as described in your letter of September 7, 2007 and reiterated in your letter of September 14, 2007. The relevant statutes and case law do not support your decision to withhold the documents that were properly subpoenaed.

While the Journals may qualify for certain protection under the Reporter's Privilege Act, 735 Ill. Comp. Stat. 5/8-901, et seq. and *Cukier v. American Medical Association*, 630 N.E.2d 1198 (Ill. App. Ct. 1994), the protection that privilege may afford does not relieve the Journals' obligation to satisfy the subpoenas at issue. As the Reporter's Privilege Act explicitly states (and as *Cukier* emphasizes) the privilege protects only the *source* of documents or information in the possession of a reporter—the Journals, not the documents or information themselves. In light of this important distinction and Pfizer's intention to discover only the documents in the Journals' possession, your use of this privilege is too broad. The Journals must, therefore, produce all documents identified in the subpoenas, and, if necessary, source information can be redacted.

Similarly, the Medical Studies Act, 735 Ill. Comp. Stat. 5/8-1201, et seq., and its common-law analog the peer-review privilege, do not protect from discovery documents in the Journals' possession, which the subpoenas seek. The Medical Studies Act evidentiary privilege extends only to hospitals, health agencies, and allied medical societies directly engaged in programs or studies designed to improve the quality of health care delivered or to reduce the rate of death or disease at a particular health care facility or medical practice. The purpose of the privilege is to promote voluntary and candid

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participation in such medical studies. *See Niven v. Siqueira*, 487 N.E.2d 937, 942 (Ill. 1985) ("[M]aterials in the hands of any legitimate medical society are protected by the [Medical Studies] Act so long as those materials were used as part of a study or program designed to improve quality control or patient care, or reduce morbidity or mortality."); *Grandi v. Shah*, 633 N.E.2d 894, 898 (Ill. App. Ct. 1994) (protected materials "must belong to a committee of a licensed or an accredited hospital or its medical staff"). Accordingly, the Journals' evaluation of third-party manuscripts does not afford them protection under this Act, especially considering that the purpose for which the Journals came into possession of the documents sought relates directly to publishing issues, not to the quality control of health care or the reduction of mortality or morbidity.

Likewise, neither the self-critical analysis privilege nor the peer-review privilege protects the Journals from their obligations under the subpoenas. By its nature and common law application, the self-critical analysis privilege does not apply to the Journals' evaluation of a third party's work product. *See Robbins v. Provena Saint Joseph Medical Center*, 2004 U.S. Dist. LEXIS 3878 (N.D.Ill. 2004). Moreover, the peer-review privilege does not apply to the Journals as the review exercises they conduct are not akin to that which the privilege contemplates. The critique and evaluation of manuscripts submitted for publication does not adversely affect the public interest in promoting candor and voluntary participation in programs designed to improve the delivery of health care or reduce mortality or morbidity rates at a hospital or medical practice.

Additionally, Federal Rule of Civil Procedure 45 requires the Journals to produce a privilege log for those documents withheld pursuant to a legitimate claim of privilege. *See* Fed.R.Civ.P 45(d)(1)(D)(2)(A) ("When information subject to a subpoena is withheld on a claim that it is privileged . . . the claim shall be made expressly and shall be supported by a description of the nature of the documents, communications, or things not produced that is sufficient to enable the demanding party to contest the claim."); *see also Pietro v. Marriott Senior Living Servs., Inc.*, 810 N.E.2d 217, 225 (Ill. App. Ct. 2004) (requiring production of a privilege log in light of privilege claim under the Medical Studies Act).

In light of this authority, I look forward to the Journals' cooperation in the production of documents sought pursuant to the subpoenas, and a privilege log for those documents for which you continue to assert privilege, without the need to resort to motions practice or unnecessarily involve the courts. Please call me with any questions or concerns.

Very truly yours,

Jennifer K. Squillario

EXHIBIT H

Squillario, Jennifer K.

From: Joseph Thornton [Joseph.Thornton@jama-archives.org]
Sent: Friday, October 26, 2007 6:41 PM
To: Squillario, Jennifer K.
Subject: continuing discussion; application to divest
Follow Up Flag: Follow up
Flag Status: Red

Jennifer Squillario, Esq..
DLA Piper
Baltimore

Dear Ms. Squillario:

I write regarding our telephone conversation on October 23. You indicated that your client [presumably all three defendants] was nterested in filing a motion to compel, if JAMA was not produce additional documents or a privilege. I thanked you for the call and terated that I was willing to discuss and keep an open mind, if you or your colleagues had additional information about the exhaustion of alternative sources for the information sought in the subpoenas, and its relevance to the remaining claims and affirmative defenses.

We believe that your and your clients have an obligation under the FRCP and the Illinois Reporters Privilege Act to articulate how the information and documents you seek of us would be relevant, probative and not cumulative in regard to the Third Amended Complaints, the Answers and the numerous pretrial and discovery orders that have been entered by Judge Breyer and the Special Master Smith.

I'll give you just one example, paragraph 16 of the Third Amended Master Bextra Complaint. The Defendants Answer admits a paper was published in an issue of Archives of Internal Medicine [AIM], deny the Plaintiffs' characterization of it and "respectfully refer the Court to the complete publication of the contents." In September I produced to you an "exhibit quality original" of the January 2005 AIM article, for that purpose. It is not obvious to me how any other material we might have would assist you or plaintiffs counsel in confirming or denying the economic injuries alleged. You know the names of the authors of that article. You can interview them or issue discovery or trial subpoenas to them. The Defendants' Answer admits that in April 2005, Pfizer agreed to suspend sales and marketing of Bextra after talks with the FDA. So what is the propriety and basis for your subpoenas asking AIM for nearly ten years worth of documents?

With scores of plaintiffs being dismissed for failing to comply with the most basis discovery orders [When did you take Bextra? For how long and how many times? Based on the prescription of which doctor?] and the Court considering fundamental Causation issues regarding whether and when and which plaintiffs can proceed, it is unduly burdensome and unreasonable for you to expect a non-party to go to the trouble and expense of producing a privilege log of documents that are irrelevant and to which you would object if offered by the plaintiffs.

You are asking us to waive or violate our asserted privileges, so you might learn the identities of peer reviewers to articles that may have been submitted but rejected, so they never saw the light of day. Why isn't that a violation of the Defendants responsibilities under FRCP 26 when the Defendants already are on record objecting to the likely testimony of plaintiffs' experts about Bextra dosage?

As previously stated, the Defendants have the burden of proof and persuasion under the Illinois statute we cited, with an application to divest being the appropriate pleading, not a motion to compel. You and your colleagues may be able to articulate compelling reasons to overcome the asserted privilege, so I remain willing to discuss any now, prior to your filing an application. If am I not persuaded, I understand it would be your right to consider compulsory compliance, but we assert the right vehicle for judicial review is set forth in 735 Ill. Comp. Stat. Ann. 5/8-901 et seq.

I understand that your clients expect you to be thorough and utilize the appropriate procedures, if meet and confer efforts fail. My hope is you will advise them that you already have been thorough in your efforts to discover relevant and potentially probative and admissible information, or that there are alternative sources that have not been exhausted that should be pursed first.

Sincerely,

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EXHIBIT I

DLA PIPER

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Jennifer K. Squillario
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T 410.580.4145
F 410.580.3145

November 19, 2007

VIA FIRST CLASS MAIL & E-MAIL

Joseph P. Thornton, Esq.
Editorial Counsel
JAMA & Archives Journals
515 North State Street
Chicago, IL 60610

Re: JAMA & Archives of Internal Medicine Subpoenas
In re: Bextra and Celebrex Marketing Sales Practices and Product Liability Litigation, MDL 1699

Dear Mr. Thornton:

This letter is intended to memorialize our telephone conversation on November 14, 2007, during which we discussed your e-mail to me dated October 26, 2007. As we discussed, Pfizer disagrees that the right vehicle for judicial review of the subpoenas to JAMA and the Archives of Internal Medicine is filing an application in state court pursuant to state law. Rather, if we are unable to reach an amicable resolution of these two subpoenas, it is Pfizer's intention to file a motion to compel in the United States District for the Northern District of Illinois.

Additionally, Pfizer disagrees that you have complied with the requirements of Federal Rule of Civil Procedure 45. Pursuant to Rule 45, you are required to produce a privilege log for those documents withheld on the basis of privilege. *See* Fed. R. Civ. Proc. 45(d)(1)(D)(2)(A) ("When information subject to a subpoena is withheld on a claim that it is privileged . . . the claim shall be made expressly and shall be supported by a description of the nature of the documents, communications, or things not produced that is sufficient to enable the demanding party to contest the claim."). The claims of privilege laid out in your September 7, 2007 letter do not satisfy this requirement. *See* WRIGHT & MILLER, FEDERAL PRAC. & PROC. ¶ 2458 (Supp. 2007) ("Courts consistently have held that such a party is required to produce a document index or privilege log, and that the failure to produce a log of sufficient detail constitutes a waiver of the underlying privilege claim.").

Further, Pfizer disagrees with your position that Pfizer must first attempt to obtain the requested information from other sources prior to seeking the requested information from JAMA and the Archives of Internal Medicine. Many, if not all, of the documents requested in the subpoena are simply not available from a source other than JAMA and the Archives of Internal

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Medicine. Also, the requested information is relevant and probative as the information contained in academic and scientific journals is at issue in the litigation.

As we have discussed at length both in writing and during telephone conversations, it is Pfizer's position that your withholding of the documents based on privilege lacks merit. Pfizer has attempted to work out a reasonable and amicable resolution, including suggesting that you redact source information—peer reviewer names—from the documents. Pfizer continues to be willing to negotiate a resolution; however, if you do not intend to produce documents other than those already produced, which consist only of copies of the published articles, Pfizer will be forced to file a Motion to Compel.

Very truly yours,

Jennifer K. Squillario

EXHIBIT J

JAMA & ARCHIVES JOURNALS
American Medical Association

Joseph P. Thornton, JD
Editorial Counsel

312 464-4609 Fax 312 464-4073
joseph.thornton@jama-archives.org

SCIENTIFIC PUBLICATIONS & MULTIMEDIA APPLICATIONS
515 North State Street Chicago, IL 60610 USA

January 11, 2008

Ms. Jennifer Squillario, Esq.
DLA Piper US, LLP
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6225 Smith Avenue
Baltimore, MD 21209-3600

Re: Objections to Subpoenas Issued to JAMA and the Archives of Internal Medicine
In re: Bextra and Celebrex Marketing Sales Practices and Product Liability Litigation, MDL 1699

Dear Ms. Squillario:

We spoke on January 3rd regarding the above subpoenas, and I offered to draft a letter documenting our discussion. I had hoped that Judge Breyer's ruling on causation, the scope of expert testimony and production by other subpoenaed entities would negate your interest in our privileged material.

I asked that you waive or withdraw Requests 2, 3, and 4, of each subpoena because they concerned editorial judgments, the peer-review process and decisions regarding rejected papers. You stated you could not bargain as to Requests 2 and 3, but would agree to accept redacted versions of documents that respond to Request 4, (i.e., JAMA could delete or redact the identifiers of the peer-reviewers from editorial manuscripts as long as we revealed their comments and notations on the various drafts). In an effort to explore whether this might develop into an acceptable compromise, I asked whether Pfizer would agree in writing to refrain from attempting to learn the identities of the peer reviewers if hypothetically so-called "redacted" manuscripts were furnished. At that point in the telephone conversation, neither of us had the authority to reach such a compromise, we simply were exploring creative alternatives.

On January 4th, you confirmed that you could so agree, which prompted me to present the idea to our Editor-in-Chief. I warned you at the time that I was new to this client and we might not view this approach as acceptable. Indeed, the Editor-in-Chief is concerned this would be a serious departure from JAMA's understanding of its responsibility to its authors, peer-reviewers and the confidential editorial process.

As to your request for a privilege log, I believe I have outlined the relevant categories of material we are withholding:

1. Correspondence to and from authors to JAMA editors throughout the editorial process of submission, consideration, revision, acceptance and publication.
2. Correspondence to, from and among editors and peer reviewers throughout the editorial process.
3. Authorship forms regarding, among other things, disclosures and representations by all co-authors regarding their role in the preparation of the manuscript, figures and tables, in the underlying research or clinical trial and any pertinent financial interest or affiliation, all for consideration by the editors in deciding whether and what to publish;
4. Various versions of manuscripts, figures and tables from submission through editing to publication.

We contend that neither Federal nor Illinois Rules of Civil Procedure require us to produce a log so detailed that it would amount to a waiver of the privileges we assert, or provide a road map for you to undermine or circumvent them.

In our penultimate conversation, I revealed that in accordance with our retention policy, we would not possess any documents associated with the two papers [Requests (e) and (f)] that you suspect might have been submitted but rejected. JAMA's retention policy for rejected items is just one year.

If you pursue a Motion to Compel and attempt to overcome our asserted privileges, we expect your filings will address:

1. The procedures, pleading and proof elements of the Illinois Reporter's Privilege Act;
2. The notion that the privileged additional material you seek is relevant, let alone probative, to any remaining claims in the Plaintiffs' Third Amended Complaint and your affirmative defenses.
3. Your duty to exhaust alternative sources for the privileged material you seek from JAMA. As I have mentioned many co-authors have relationships with the defendants. They would posses some of this material and may be under a contractual obligation to Pfizer to produce it upon request.
4. Your duty to demonstrate how the material you seek goes to the heart of the pending case in which the subpoenas were issued.

Our published articles may have been read by the Plaintiffs' attending physicians or expert witnesses, but we fail to see how the privileged, confidential and unpublished material generated during the editorial process could have influenced the prescribing decisions of any doctor or enticed any plaintiff to request or refrain from taking Bextra or Celebrex.

While the published material we furnished to you in September 2007 is self-authenticating under the Federal Rules, the privileged material is useless without the context and authenticity that only a witness could provide. Your subpoenas were issued with deposition notices, and if we were compelled to produce additional documents, our designated 30 (b)(6) witness would be Catherine D. DeAngelis, MD, MPH, Editor-in-Chief of both JAMA and the Archives Journals, including the Archives of Internal Medicine.

We renew and do not waive any objections and arguments more fully set forth in previous letters and emails. If you decide to proceed further with a Motion to Compel, I trust you or local Chicago counsel Matthew Sullivan will consult me on an agreeable return date for an initial hearing and a briefing schedule.

Sincerely,

Joseph P. Thornton

Joseph P. Thornton